PSJ2 Exh 46

Pain MANAGEMENT

Nonmalignant Pain

PRESENTATION INSTRUCTIONS FOR THE REPRESENTATIVE

When presenting this slide kit, two options exist:

Option #1

Present the slide kit sequentially and in its entirety.

Option #2

If there is a time constraint factor, the kit must be presented in three parts as defined below:

Part #1: 1-22
Part #2: 23-41
Part #3*: 42-57

*Slides 33-37 must be presented in conjunction with Part #3 for fair balance.

Presentation of slides in any way other than as outlined by the above options is strictly prohibited.

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What is Nonmalignant Pain?

- Pain not related to cancer
- Pain associated with a disease such as:
  - myofascial, neuropathic, and complex regional pain syndromes
  - arthritis
  - headache
  - low back pain

(Haythornthwaite JA et al. *J Pain Symptom Manage.* 1998)
(Ellison NM et al. *Patient Care,* 1998)

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Slide References

Haythornthwaite JA, Menefee LA, Quatrano-Piacentini AL, Pappagallo M. Outcome of chronic opioid therapy for non-cancer pain. *J Pain Symptom Manage* 1998;15:185-194.

Ellison NM, Lipman AG, Patt RB, Portenoy RK. Opioid analgesia: an essential tool in chronic pain. *Patient Care* 1998:2-11.

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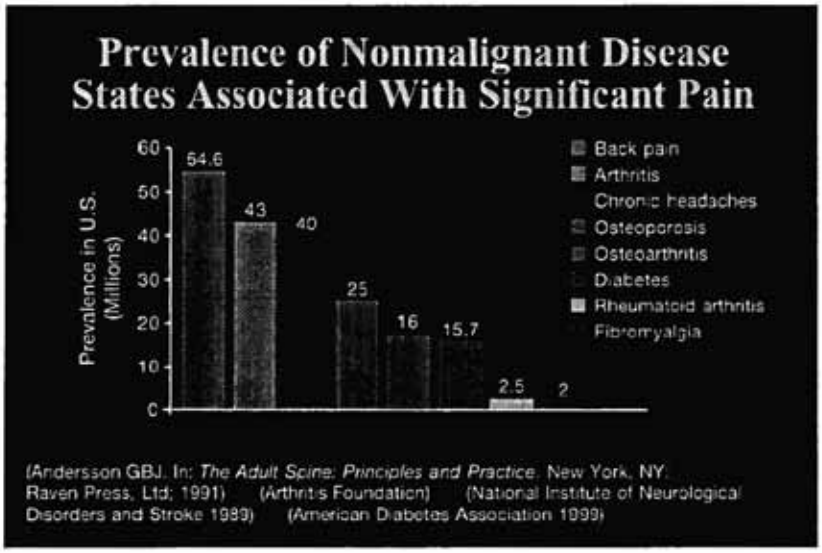

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A number of disease states are associated with significant pain.

- ***Back pain*** has a general yearly prevalence of 15% to 20% of the American population.[1] It is the second most common reason for visiting the primary care physician and the most common cause of disability for people younger than 45 years of age.[1]
- ***Arthritis*** afflicts nearly 43 million Americans,[2] with 16 million people suffering from osteoarthritis,[3] 2.5 million people suffering from rheumatoid arthritis,[4] and 2 million people suffering from fibromyalgia.[2]
- ***Chronic headaches*** afflict 40 million people in this country.[5]
  - migraines alone account for more than 65 million lost workdays each year[5]
- ***Osteoporosis and diabetes***, conditions that affect a considerable portion of the population, are both associated with painful sequelae.
  - osteoporosis is responsible for more than 1.5 million painful bone fractures each year[6]
  - between 60% to 70% of diabetics experience some form of nerve damage, resulting in painful neuropathies and, if severe enough, can result in lower limb amputation[7]

[1]Andersson GBJ. The epidemiology of spinal disorders. In: Frymoyer JW, ed. *The Adult Spine: Principles and Practice*. Volume one. New York, NY: Raven Press, Ltd; 1991:107-146.
[2]Arthritis fact sheet. [Arthritis Foundation web site]. Available at: http://www.arthritis.org/resource/fs/arthritis.asp.
[3]Arthritis Foundation. *Osteoarthritis* [brochure]. Atlanta, GA: Arthritis Foundation; 1997.
[4]Arthritis Foundation. *Rheumatoid Arthritis* [brochure]. Atlanta, GA: Arthritis Foundation; 1998.
[5]National Institute of Neurological Disorders and Stroke. *Chronic Pain: Hope Through Research*. [National Institutes of Health web site]. November 1989. Available at: http://www.nih.gov/health/chip/ninds/cronpain/.
[6]Arthritis Foundation. *Osteoporosis* [brochure]. Atlanta, GA: Arthritis Foundation; 1997.
[7]Diabetes facts and figures. [American Diabetes Association web site]. 1999. Available at: http://www.diabetes.org/ada/facts.asp.

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Andersson GBJ. The epidemiology of spinal disorders. In: Frymoyer JW, ed. *The Adult Spine: Principles and Practice.* Volume one. New York, NY: Raven Press, Ltd; 1991:107-146.

Arthritis fact sheet. [Arthritis Foundation web site]. Available at: http://www.arthritis.org/resource/fs/arthritis.asp.

National Institute of Neurological Disorders and Stroke. *Chronic Pain: Hope Through Research.* [National Institutes of Health web site]. November 1989. Available at: http://www.nih.gov/health/chip/ninds/cronpain/.

Arthritis Foundation. *Osteoporosis* [brochure]. Atlanta, GA: Arthritis Foundation; 1997.

Arthritis Foundation. *Osteoarthritis* [brochure]. Atlanta, GA: Arthritis Foundation; 1997.

Diabetes facts and figures. [American Diabetes Association web site]. 1999. Available at: http://www.diabetes.org/ada/facts.asp.

Arthritis Foundation. *Rheumatoid Arthritis* [brochure]. Atlanta, GA: Arthritis Foundation; 1998.

Arthritis fact sheet. [Arthritis Foundation website]. Available at: http://www.arthritis.org/resource/fs/arthritis.asp.

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Nonmalignant pain may be classified as acute or chronic. Chronic pain is distinguished from acute pain not only by the longer duration of pain, but by the body's inability to restore its physiological functions to normal homeostatic levels.[8]

Acute pain results from injury of body tissue.[8] Healing occurs within a few days or a few weeks because the injury does not overwhelm the body's reparative mechanisms.[8] Although medical intervention is not necessary for healing to occur, many patients with acute pain do seek medical care to speed up the healing process by shortening the duration of the injury.[8] The primary goal of therapy should be to reduce or eliminate the pain by treating the underlying injury.

Chronic pain is triggered by an injury or disease that often exceeds the body's capability for healing.[8] For example, the injury may cause damage to the nervous system to the extent that it is unable to restore itself to a normal state.[8] Chronic pain can be a multidimensional experience with stress, environmental and affective factors all contributing to the persistence and intensity of the pain.[8] Patients with chronic pain seek medical attention, however, they are often inadequately treated.[8] Unlike acute pain, chronic pain is unrelenting and will persist with cessation of therapy.[8]

[8]Loeser JD, Melzack R. Pain: an overview. *Lancet* 1999;353:1607-1609.

Slide Reference
Loeser JD, Melzack R. Pain: an overview. *Lancet* 1999;353:1607-1609.

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The American Pain Society (APS) published *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain* in 1999.[9] In regard to the management of acute pain, this guide states that "drug therapy is the mainstay of treatment" and classifies drugs into three categories: non-opioid analgesics, opioid analgesics, and analgesic adjuvants.[9]

The APS indicates that a non-opioid should be included in any analgesic regimen, even if pain is severe enough to require the addition of an opioid.[9]

Opioid analgesics should be added to non-opioids to manage acute pain that does not respond to non-opioids alone.[9] The APS makes the following recommendations in regard to the use of opioids[9]:

- Follow patients closely, particularly when beginning or changing analgesic regimens
- Watch for the development of tolerance and treat appropriately
- Be aware of physical dependence and prevent withdrawal
- Do not label a patient addicted if they are physically dependent on or tolerant to opioids
- Be alert to the psychological state of the patient

Analgesic adjuvants can be added at any time in the patient's pain treatment program to[9]:

- Enhance analgesic effects of opioids or aspirin-like drugs
- Provide independent analgesic activity
- Counteract the side effects of analgesics

[9]American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain*. 4th ed. Glenview, IL: American Pain Society; 1999.

Slide Reference
American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain*. 4th ed. Glenview, IL: American Pain Society; 1999.

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Pharmacologic Management of Chronic Nonmalignant Pain: A Controversial Issue

While opioid therapy has been medically and ethically accepted for the management of malignant pain and acute pain, major controversies continue to surround the use of opioids for chronic, nonmalignant pain

(Pappagallo M, Heinberg LJ. *Semin Neurol*, 1997)

According to Russell Portenoy, chairman of pain medicine and palliative care at Beth Israel Medical Center in New York, opioids are among the most stigmatized medicines. There are many myths and misconceptions that physicians and the public perceive.[10]

The practice of prescribing long-term opioids for patients with chronic nonmalignant pain is controversial.[11,12] Unlike acute and malignant pain, opioid therapy for chronic nonmalignant pain is not time-limited or necessarily limited to a specific underlying condition. A lack of controlled clinical trials to support the role of opioid therapy for nonmalignant pain has caused healthcare professionals to act on the cultural image of pain rather than on scientific knowledge.[13] Healthcare professionals are often influenced by societal forces that inhibit the treatment of chronic nonmalignant pain. These forces may include[14]:

- Fear of patient addiction to opioids
- Misconceptions regarding the development of tolerance
- Mistrust that patients will abuse/divert pain medications
- Lack of formal training of physicians, nurses, and pharmacists in concepts of pain management
- Fear by physicians that they will be reported to medical review boards for investigation and prosecution when they prescribe strong pain medications
- Fear of side effects

Truthfully, opioids can be a useful long-term treatment for chronic nonmalignant pain.[15] Patients may be maintained on chronic opioid therapy without developing unmanageable side effects, tolerance, or substance abuse problems.[15,11]

[10]Hendricks M. Just give me something for the pain. *Johns Hopkins Magazine* 1999. Available at: http://www.jhu.edu/~jhumag/0699web/pain.html.
[11]Turk DC, Brody MC, Okifuji EA. Physicians' attitudes and practices regarding the long-term prescribing of opioids for non-cancer pain. *Pain* 1994;59:201-208.
[12]Pappagallo M, Heinberg LJ. Ethical issues in the management of chronic nonmalignant pain. *Semin Neurol* 1997;17:203-211.
[13]Hill CS. When will adequate pain treatment be the norm? *JAMA* 1995;274:1881-1882.
[14]Holmquist GL. The appropriate use of opioids in the management of chronic pain: a pharmacist's perspective. *Pharmacy Times* 1999;29:3-11.
[15]Fuchs PN, Gamsa A. Chronic use of opioids for nonmalignant pain: a prospective study. *Pain Res Manage* 1997;2:101-107.

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Pappagallo M, Heinberg LJ. Ethical issues in the management of chronic nonmalignant pain. *Semin Neurol* 1997;17:203-211.

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The issue of complexity contributes to the the controversy that surrounds the pharmacologic management of nonmalignant pain. Healthcare professionals are often challenged with untangling the web of ailments that can occur with chronic pain.[10] The goals of therapy for chronic nonmalignant pain must include achieving a satisfactory level of pain relief for the patient, while at the same time, preserving the patient's ability to function—to drive, work, care for children, or perform other ordinary tasks of daily living.[16] Success of treatment should be measured by physical function, as well as by improvements in mood or social interaction.[16]

Fear that side effects may adversely impact a patient's functional ability often results in the withholding of opioids for the patient with chronic pain.[14] However, the side effects that most often lead to discomfort in a patient's life—constipation, nausea, and drowsiness—can often be addressed with simple preventive treatments.[14]

[10]Hendricks M. Just give me something for the pain. *Johns Hopkins Magazine* 1999. Available at: http://www.jhu.edu/~jhumag/0699web/pain.html.
[16]Ellison NM, Lipman AG, Patt RB, Portenoy RK. Opioid analgesia: an essential tool in chronic pain. *Patient Care* 1998:2-11.
[14]Holmquist GL. The appropriate use of opioids in the management of chronic pain: a pharmacist's perspective. *Pharmacy Times* 1999;29:3-11.

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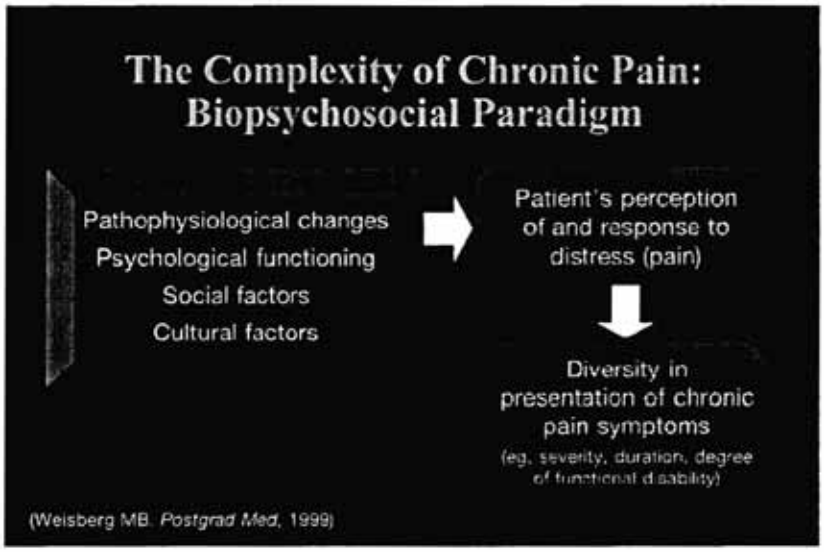
Belgrade MJ. Opioids for chronic nonmalignant pain. *Postgrad Med* 1999;106:115-122.
Marcus DA. Treatment of nonmalignant chronic pain. *Am Fam Phys* 2000;61:1331-1338, 1345-1346.

Nonmalignant Pain



The biopsychosocial model of disease recognizes the complex interplay of pathophysiologic changes, psychological functioning, and the social and cultural factors on the presentation of pain symptoms by the patient with chronic, nonmalignant pain.[17] These attributes of a patient's being affect how the patient perceives and responds to distress, that is pain, and account for the diversity in presentation of the patient's symptoms (eg, severity, duration, degree of functional ability).[17]

[17]Weisberg MB. Why is chronic pain so difficult to treat? *Postgrad Med* 1999;106:141-164.

Slide Reference
Weisberg MB. Why is chronic pain so difficult to treat? *Postgrad Med* 1999;106:141-164.

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Effects of Chronic Pain on Quality of Life

Healthcare professionals must assess how pain impacts a patient's life and what the patient's life was like before the pain

Identify how pain affects your patient's:

- Sleep
- Household chores
- Mood
- Work tasks
- Leisure interests

(Schneider JP. *J Care Manage*, 1998) (Marcus DA. *Am Fam Phys*, 2000)

9

Patients with chronic pain report impairments of multiple quality-of-life measures[18]:

- Physical
- Social
- Psychological

The goal of pain management is the reduction of pain which often leads to improvements in key areas of a patient's life—function, sleep, and mood.[18]

[18]Marcus DA. Treatment of nonmalignant chronic pain. *Am Fam Phys* 2000;61:1331-1338, 1345-1346.

Slide References

Schneider JP. Management of chronic non-cancer pain: a guide to appropriate use of opioids. *J Care Manage* 1998;4:10-22.
Marcus DA. Treatment of nonmalignant chronic pain. *Am Fam Phys* 2000;61:1331-1338, 1345-1346.

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Pain is associated with extensive comorbidity. Fifty-eight percent of chronic pain patients experience coexisting symptoms of depression or anxiety.[18] When developing a pain management plan, healthcare professionals should address comorbid diseases in an effort to improve a patient's functional ability.[18] Coexisting diseases may impact a patient's perception and complaints of pain, and ability to participate in treatment.[18]

The American Society of Consultant Pharmacists reported on the comorbidities among residents of long-term care facilities who experience chronic pain.[19] Among residents in pain[19]:

- 32% experienced depression
- 26% experienced anxiety
- 12% indicated impaired memory

In addition, 54% expressed a diminished ability to enjoy social activities.[19]

[18]Marcus DA. Treatment of nonmalignant chronic pain. *Am Fam Phys* 2000;61:1331-1338, 1345-1346.
[19]American Society of Consultant Pharmacists. Management of chronic non-malignant pain. Symposia highlights. May 18, 1998.

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Marcus DA. Treatment of nonmalignant chronic pain. *Am Fam Phys* 2000;61:1331-1338, 1345-1346.

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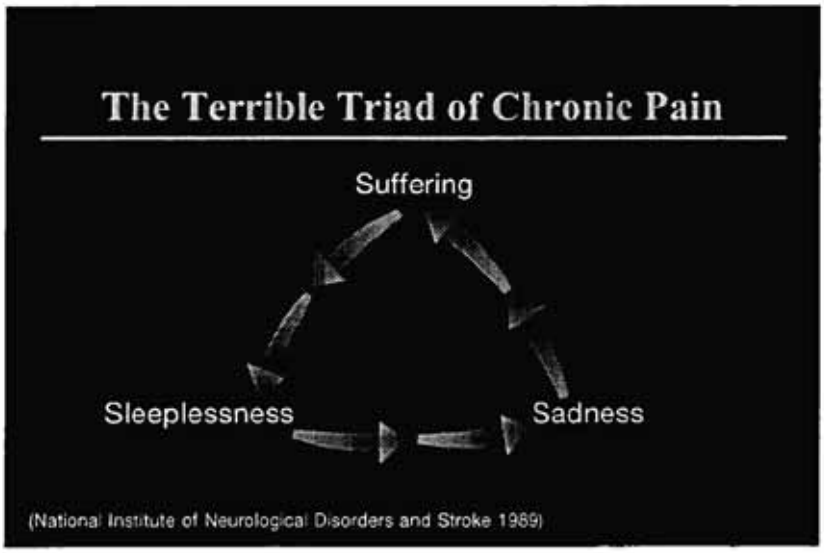

Chronic pain patients often become victims of a vicious cycle referred to as the "terrible triad."[5] This continuous cycle of suffering, sleeplessness, and sadness may occur in patients when pain limits their ability to work, their appetite, and the amount of physical activity they can endure.[5] When pain interferes with a patient's ability to function, the patient may experience a total preoccupation with the pain which may lead to irritability, depression, and loss of sleep.[5] The "terrible triad" can not only consume a patient's quality of life, but it can also greatly impact the patient's family and caregivers.

[5]National Institute of Neurological Disorders and Stroke. *Chronic Pain: Hope Through Research.* [National Institutes of Health web site]. November 1989. Available at: http://www.nih.gov/health/chip/ninds/cronpain/.

Slide Reference
National Institute of Neurological Disorders and Stroke. *Chronic Pain: Hope Through Research.* [National Institutes of Health web site]. November 1989. Available at: http://www.nih.gov/health/chip/ninds/cronpain/.

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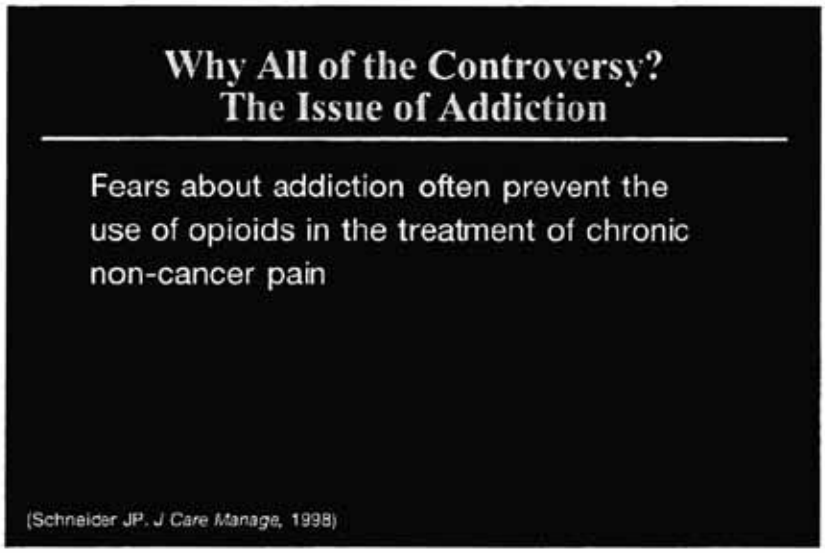

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Fears attributed to lack of education of healthcare professionals often hinder the use of opioid medications for the treatment of chronic nonmalignant pain and contribute to the controversy surrounding this issue.[20]

It is imperative that healthcare professionals understand the meanings of the terms addiction, physical dependence, tolerance, and pseudoaddiction, and that they are able to distinguish the differences between them.

Addiction[20]

- A psychological and behavioral disorder characterized by:
  - loss of control (compulsive use)
  - continuation of drug use despite adverse consequences
  - preoccupation with obtaining and using the drug despite the presence of adequate analgesia

Physical Dependence[12]

- Characterized by the occurrence of a withdrawal syndrome when there is a sudden cessation in the use of the medication
- Relatively common with opioids and steroids
- Does not signify addiction

Tolerance

- Characterized by the need for dose escalation to maintain the same drug-related effect[12]
- Patients do not usually develop significant tolerance to opioid analgesia[20]
  - requests for dose escalation can be due to increased physical activity, worsening physical problems, or deterioration in psychological state

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Pseudoaddiction

- Phenomenon characterized by a pattern of drug-seeking behavior due to inadequate pain management[21]
  - patient mislabeled as an addict[20]
  - unnecessary withholding of opioid medications occurs[20]
- Phenomenon prevented by administration of opioids on a regular basis at doses that provide more "pain prophylaxis"[22]

[20]Schneider JP. Management of chronic non-cancer pain: a guide to appropriate use of opioids. *J Care Manage* 1998;4:10-22.
[12]Pappagallo M, Heinberg LJ. Ethical issues in the management of chronic nonmalignant pain. *Semin Neurol* 1997;17:203-211.
[21]Federation of State Medical Boards of the United States, Inc. *Model Guidelines for the Use of Controlled Substances for the Treatment of Pain*. Euless, TX: Federation of State Medical Boards of the United States, Inc; 1998.
[22]Zenz M, Strumpf M, Tryba M. Long-term oral opioid therapy in patients with chronic nonmalignant pain. *J Pain Symptom Manage* 1992;7:69-77.

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Schneider JP. Management of chronic non-cancer pain: a guide to appropriate use of opioids. *J Care Manage* 1998;4:10-22.

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Patient Barriers

- Most Americans would rather bear pain than take action to relieve it
  - 92% believe that pain is a fact of life
  - 82% think that it is too easy to become reliant on pain medication
  - 72% believe that medication will not be effective with continued use
  - 46% avoid medication until pain becomes bad

(Bostrom M. *J Pain Symptom Manage*, 1997)

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Barriers to pain management exist for patients. The results of the Mayday Fund survey indicate that "Americans would rather bear pain that take action to relieve it."[23] Ninety-two percent of survey respondents agreed that pain is a fact of life.[23] Given this belief in the inevitability of pain, many patients try to be stoic, do not ask for pain-relieving medication, and believe that they should not complain to healthcare professionals.[24] Many people believe that medication will become ineffective if used too often and express concern about dependency and addiction.[23]

[23]Bostrom M. Summary of the Mayday Fund Survey: public attitudes about pain and analgesics. *J Pain Symptom Manage* 1997;13:166-168.
[24]American Pain Foundation. Painful facts. [American Pain Foundation web site]. 1999. Available at: http://www.painfoundation.org/painful.htm.

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Bostrom M. Summary of the Mayday Fund Survey: public attitudes about pain and analgesics. *J Pain Symptom Manage* 1997;13:166-168.

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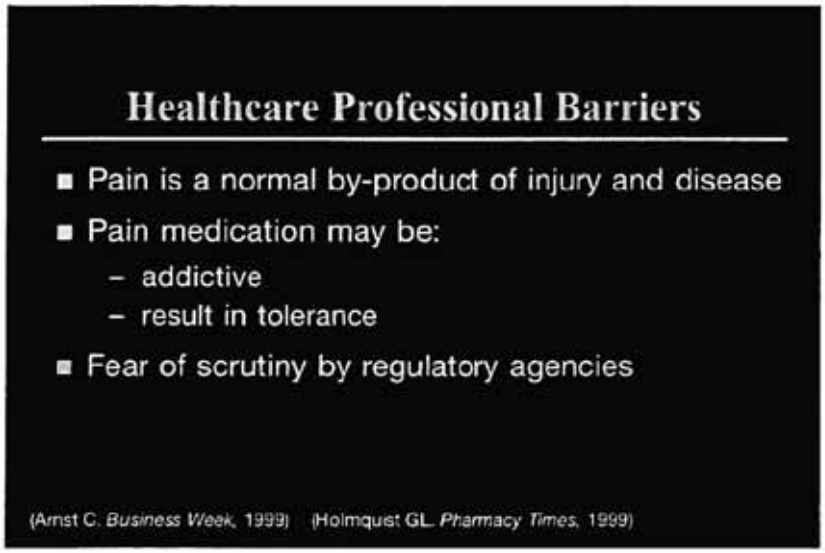

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Other barriers to effective pain management include misguided beliefs and fears held by healthcare professionals. Many physicians consider pain to be a normal by-product of injury and disease, and assume that pain will resolve itself with treatment of the underlying condition.[25] On the contrary, current pain research suggests that pain should be treated as a disease in and of itself, independent of underlying cause.[25]

The fear of addiction to painkillers hinders therapeutic use of valuable medications, particularly opioids.[14] Addictive behaviors rarely occur in patients who use opioids under medical care for pain relief, especially those with no prior history of substance abuse.[14]

Healthcare professionals fear that by prescribing strong pain relievers for nonmalignant pain, they may trigger scrutiny by regulatory agencies.[14] Physicians fear they may be reported for investigation to medical review boards and may subsequently be the target of prosecution and punitive sanctions.[14]

All of these beliefs and fears result in a tendency to inadequately treat pain of nonmalignant origin.

[25]Arnst C. Conquering pain: new discoveries and treatments offer hope. *BusinessWeek* [serial online] March 1, 1999. Available at: http://www.businessweek.com/1999/99_09/b3618001.htm.
[14]Holmquist GL. The appropriate use of opioids in the management of chronic pain: a pharmacist's perspective. *Pharmacy Times* 1999;29:3-11.

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Arnst C. Conquering pain: new discoveries and treatments offer hope. *BusinessWeek* [serial online] March 1, 1999. Available at: http://www.businessweek.com/1999/99_09/b3618001.htm.
Holmquist GL. The appropriate use of opioids in the management of chronic pain: a pharmacist's perspective. *Pharmacy Times* 1999;29:3-11.

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Pharmacist Barriers

- Lack of education
  - 33% of pharmacists believed a patient will become addicted if opioids are taken daily for one month
  - 42% of pharmacists reported addiction was physical dependence, tolerance, and psychological dependence
  - 47.2% of pharmacists thought the practice of prescribing opioids for more than several months for nonmalignant pain should be discouraged

(Greenwald BD, Narcessian EJ. *J Pain Symptom Manage*, 1999)

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Confusion between legitimate and illegitimate use of medication and outdated regulatory policies discourage the prescribing of pain medication and perpetuate the undertreatment of pain.[26]

A survey of 52 randomly selected New Jersey community pharmacists (69% response rate) showed that lack of education of terminology and concerns about federal or state investigations constituted barriers to stocking and prescribing opioids.[26] The study concluded that pharmacists, like many other healthcare professionals, could benefit from education regarding issues related to the use of opioids for chronic pain.[26]

(Note: This text also supports information on the next slide)

[26]Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns. *J Pain Symptom Manage* 1999;17:369-375.

Slide Reference

Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns. *J Pain Symptom Manage* 1999;17:369-375.

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Pharmacist Barriers (cont'd)

- Fear
  - 17% of pharmacists surveyed reported moderate to complete reluctance to stock opioids due to concerns about federal or state investigations
- Bias
  - 51% of NYC pharmacies in predominately non-white neighborhoods did not stock sufficient opioids to treat patients with severe pain

(Greenwald BD, Narcessian EJ. *J Pain Symptom Manage*. 1999)
(Morrison RS et al. *N Engl J Med*, 2000)

16

A survey of a randomly selected sample of 30% of New York City pharmacies was conducted to obtain information about their stock of opioids.[27]

- Survey response rate: 81% (347 of 431)
- 51% of the pharmacies did not have sufficient supplies of opioids to treat patients with severe pain
- In predominately nonwhite neighborhoods, only 25% of pharmacies had sufficient opioid supplies to treat patients in severe pain
- In predominately white neighborhoods, 72% of pharmacies had sufficient opioid supplies to treat patients in severe pain

The results of this survey suggest that nonwhite patients may be at greater risk for the undertreatment of pain than white patients. Furthermore, it can be concluded from this study that bias plays a role in the practices of healthcare professionals with regard to opioid medications.[27]

[27]Morrison RS, Wallenstein S, Natale DK, Senzel RS, Huang L. "We don't carry that"— failure of pharmacies in predominately nonwhite neighborhoods to stock opioid analgesics. *N Engl J Med* 2000;342:1023-1026.

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Morrison RS, Wallenstein S, Natale DK, Senzel RS, Huang L. "We don't carry that"— failure of pharmacies in predominately nonwhite neighborhoods to stock opioid analgesics. *N Engl J Med* 2000;342:1023-1026.
Greenwald BD, Narcessian EJ. Opioids for managing patients with chronic pain: community pharmacists' perspectives and concerns. *J Pain Symptom Manage* 1999;17:369-375.

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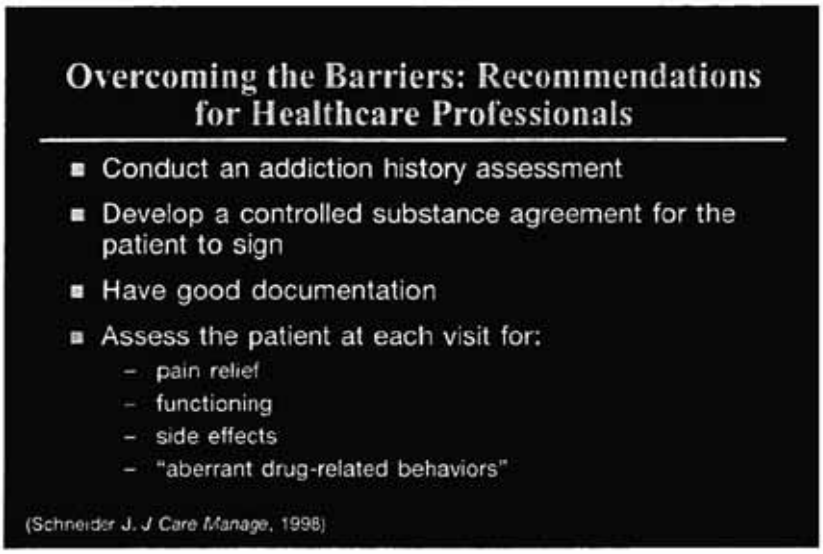

17

Establishing a standard set of procedures can assist healthcare professionals in overcoming the obstacles to opioid therapy for the management of chronic nonmalignant pain.

Conduct an addiction history assessment[20]

- Question the patient about present and past use of alcohol and/or other legal and illegal drugs
- Inquire about a family history of alcoholism and/or other addictions
- Obtain records from other treating clinicians
- Examine the patient for physical signs that support the addiction history (eg, deformities, scars)
- Be alert to the following signs of addiction:
  - unreliable drug-taking behavior
  - loss of control over drug use
  - drug-seeking behavior
  - abuse of drugs other than prescription drugs
  - contact with street drug culture
  - negative consequences resulting from drug use

Develop a controlled substance agreement for the patient to sign[20]

- Identify your expectations
- Identify the patient's responsibilities to:
  - obtain pain-related medication only from you
  - fill opioid prescriptions at one pharmacy only
  - change dose only after notifying you
  - not request early refills
  - obtain any consultations you recommend

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- abstain from alcohol and illegal drug use
- undergo urine drug screens when asked

Document everything to avoid problems with medical licensing boards[20]

- Reason patient has been prescribed an opioid
- Extensive details of the initial evaluation
- Opioid contract
- Assessments conducted at each visit
- Every prescription
- Every deviation from a prescription (eg, expected date, amount)

Assess the patient at each visit[16,20]

- Is the patient getting a significant level of analgesia?
- How are the patient's physical and psychological capabilities?
- Does the patient enjoy a higher level of functioning in daily activities than before therapy commenced?
- Does the patient have opioid-related side effects that cannot be easily managed?
- Can you recognize any aberrant drug-related behaviors?

[20]Schneider JP. Management of chronic non-cancer pain: a guide to appropriate use of opioids. *J Care Manage* 1998;4:10-22.
[16]Ellison NM, Lipman AG, Parr RB, Portenoy RK. Opioid analgesia: an essential tool in chronic pain. *Patient Care* 1998:2-11.

Slide Reference
Schneider JP. Management of chronic non-cancer pain: a guide to appropriate use of opioids. *J Care Manage* 1998;4:10-22.

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"The undertreatment of pain in today's society is not justified. This joint consensus statement has been produced pursuant to the missions of both organizations, to help foster a practice environment in which opioids may be used appropriately to reduce needless suffering from pain."

(AAPM and APS 1997)

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A 1997 consensus statement issued by the American Academy of Pain Medicine (AAPM) and the American Pain Society (APS) draws attention to the fact that "there is currently no nationally accepted consensus for the treatment of chronic pain not due to cancer."[28] The intended purpose of the statement is to serve as a guide for practitioners and regulators with regard to the judicious use of opioids in the course of medical practice relative to the treatment of chronic nonmalignant pain.[28] The consensus statement recognizes that pain is often managed inadequately and recommends that the prescribing of opioids should be guided by principles of good medical practice (ie, patient evaluation, treatment planning, consultation with pain specialists, reviews of treatment efficacy, and documentation).[28]

While no nationally accepted guidelines exist for the treatment of chronic nonmalignant pain, several organizations have joined the AAPM and APS in recognizing the need to speak out on the issue.

[28]American Academy of Pain Medicine and the American Pain Society. The use of opioids for the treatment of chronic pain [consensus statement]. Glenview, IL: American Academy of Pain Medicine and the American Pain Society; 1997.

Slide Reference

American Academy of Pain Medicine and the American Pain Society. The use of opioids for the treatment of chronic pain [consensus statement]. Glenview, IL: American Academy of Pain Medicine and the American Pain Society; 1997.

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The Council on Scientific Affairs (CSA) of the American Medical Association (AMA) issued Report 11 in 1999 which addressed the issue of opioid use in chronic noncancer pain.[29] The CSA conducted a review of the literature from 1966 through June of 1999 that concentrated on studies using human subjects relative to opioid analgesics, pain, and chronic disease.[29,30] Additional information was obtained from the web sites of various pain organizations and recently published textbooks.[29,30]

According to Report 11, the CSA determined the following based on the published data[29,30]:

- Peripheral tissue or nerve damage may lead to long-term changes that cause persistent pain in the absence of ongoing stimulation.
- Opioids are effective in treating selected patients with chronic pain not related to cancer.
- Patients most likely to benefit from opioids are those whose pain has an identifiable cause.
- The risk of addiction is increased if a patient has a history of substance abuse but addiction seems to occur infrequently in other patients.
- Physicians' fears or regulatory scrutiny play a part in the undertreatment of pain.

The CSA summarized its findings in the conclusion that "a subgroup of patients with chronic, noncancer pain can benefit from long-term opioid treatment."[29,30] As a result of this conclusion, the CSA offered recommendations regarding barriers to pain management and the promotion of educational programs on pain evaluation, treatment, and management. These recommendations were adopted as AMA policy at the 1999 AMA annual meeting.[29]

[29]Report 11 of the Council on Scientific Affairs (A-99). Use of opioids in chronic noncancer pain. [American Medical Association web site]. 1999. Available at: http://www.ama-assn.org/med-sci/csa/1999/opioids.htm.
[30]Dickinson BD, Altman RD, Nielsen NH, Williams MA for the Council on Scientific Affairs. Use of opioids to treat chronic, noncancer pain. *West J Med* 2000;172:107-115.

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Report 11 of the Council on Scientific Affairs (A-99). Use of opioids in chronic noncancer pain. [American Medical Association web site]. 1999. Available at: http://www.ama-assn.org/med-sci/csa/1999/opioids.htm.

Nonmalignant Pain

The AMA Takes Action: "Use of Opioids in Chronic Noncancer Pain" (cont'd)

Report 11 of the Council on Scientific Affairs (CSA) of the AMA

- The AMA and relevant specialty societies will promote educational offerings for physicians to facilitate learning about principles of pain diagnosis and treatment
- The AMA encourages appropriate education in pain evaluation and management to be provided as an integral part of the core curriculum at all medical schools

(AMA 1999)

Slide Reference

Report 11 of the Council on Scientific Affairs (A-99). Use of opioids in chronic noncancer pain. [American Medical Association web site]. 1999. Available at: http://www.ama-assn.org/med-sci/csa/1999/opioids.htm.

Nonmalignant Pain

"The Board recognizes that controlled substances, including opioid analgesics, may be essential in the treatment of acute pain due to trauma or surgery and chronic pain, whether due to cancer or non-cancer origins."

(Federation of State Medical Boards of the United States 1998)

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The Federation of State Medical Boards of the United States, Inc. issued *Model Guidelines for the Use of Controlled Substances for the Treatment of Pain* in May 1998 for use by state medical boards and other healthcare regulatory agencies. These guidelines focus on[21]:

- Encouraging the medical community to adopt consistent standards
- Promoting the public health by facilitating the provision of adequate and effective pain control
- Educating the medical community on treating chronic pain within the bounds of professional practice (ie, patient evaluation, treatment planning, consent and agreement for treatment, periodic review of treatment, consultation, accurate and complete medical records, and compliance with controlled substances laws and regulations)

Section I of the guidelines includes a statement by the Board recognizing that "controlled substances, including opioid analgesics, may be essential in the treatment of acute pain due to trauma or surgery and chronic pain, whether due to cancer or noncancer origins."[21] Also stated is that "physicians should not fear disciplinary action from the Board or other state regulatory or enforcement agency for prescribing, dispensing, or administering controlled substances, including opioid analgesics, for a legitimate medical purpose and in the usual course of professional practice."[21]

The Board developed these guidelines in an effort to:

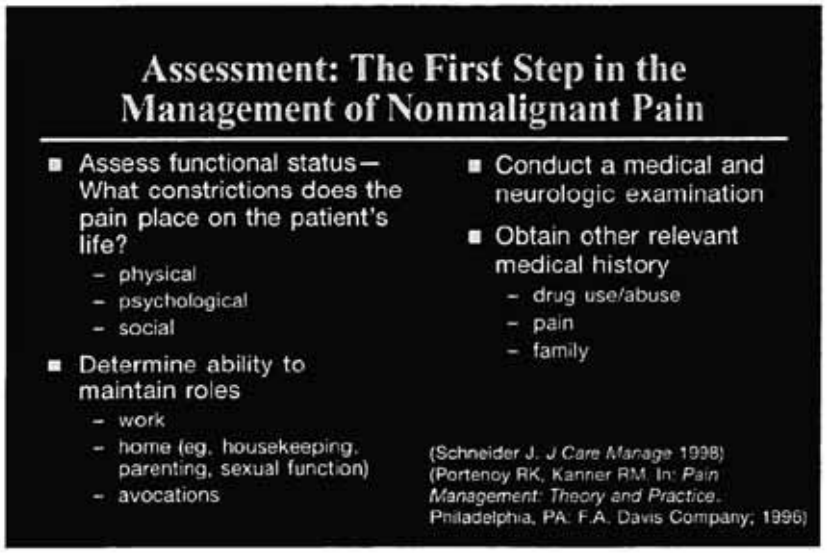
- Protect legitimate medical uses of controlled substances
- Prevent drug diversion
- Eliminate inappropriate prescribing practices

[21]Federation of State Medical Boards of the United States, Inc. *Model Guidelines for the Use of Controlled Substances for the Treatment of Pain*. Euless, TX: Federation of State Medical Boards of the United States, Inc; 1998.

Slide Reference

Federation of State Medical Boards of the United States, Inc. *Model Guidelines for the Use of Controlled Substances for the Treatment of Pain*. Euless, TX: Federation of State Medical Boards of the United States, Inc; 1998.

Nonmalignant Pain



22

Assessment of the affective and functional components of pain is an essential first step in determining the best therapeutic strategy for the management of chronic nonmalignant pain.[31]

Assess functional status[31]

- *Physical:* specific impairments, "up time," walking distance, ability to lift, sleep quality, appetite, weight
- *Psychological:* past and present psychological disorders, coping style, adaptation, personality variables, reactions to past illnesses
- *Social:* family disturbances, intimacy, involvement in litigation or compensation systems

Determine ability to maintain roles[31]

- Work
- Housekeeping tasks
- Parenting
- Daily living
- Sexual function
- Avocations

Conduct a medical and neurologic examination[31]

- Clarify the relationship between the pain and any underlying disease

Obtain other relevant medical history[31]

- Drug use
- Chronic pain
- Family history of chronic disease, chronic pain, psychiatric disease, substance abuse

[31]Portenoy RK, Kanner RM. Definition and assessment of pain. In: *Pain Management: Theory and Practice.* Philadelphia, PA: F.A. Davis Company; 1996:3-18.

Slide References

Portenoy RK, Kanner RM. Definition and assessment of pain. In: *Pain Management: Theory and Practice.* Philadelphia, PA: F.A. Davis Company; 1996:3-18.

Schneider JP. Management of chronic non-cancer pain: a guide to appropriate use of opioids. *J Care Manage* 1998;4:10-22.

Nonmalignant Pain

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"The first line direct strategy for controlling most pain is reassurance, maintenance of activity, and pharmacologic analgesia."[32] The three categories of analgesic medications include[33]:

- Non-opioid analgesics
- Opioid analgesics
- Adjuvant analgesics

[32]Caudill MA, Holman GH, Turk D. Effective ways to manage chronic pain. *Patient Care* 1996;30:154-172.
[33]Portenoy RK. Current pharmacotherapy of chronic pain. *J Pain Symptom Manage* 2000;19:S16-S20.

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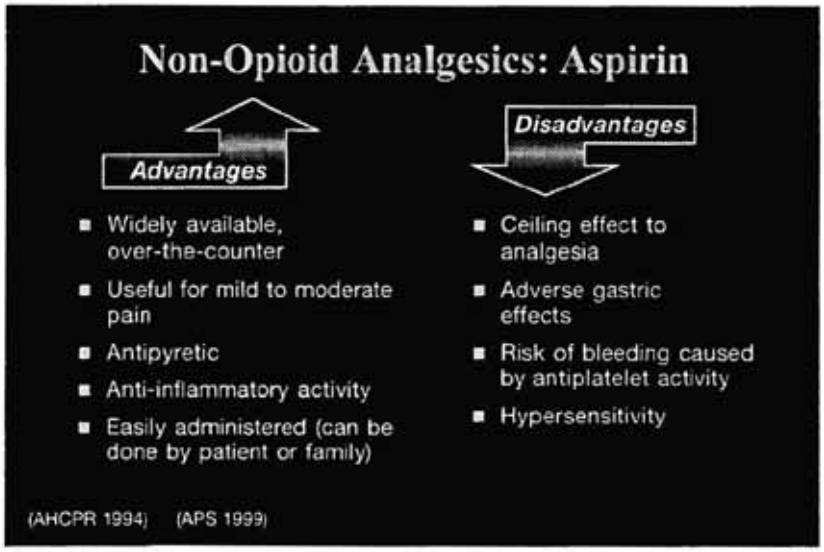
Portenoy RK. Current pharmacotherapy of chronic pain. *J Pain Symptom Manage* 2000;19:S16-S20.

Nonmalignant Pain



Aspirin is one of the world's oldest non-opioid oral analgesics.[9] It is widely available and inexpensive.[34] Aspirin's efficacy has been proven over time for a wide variety of mild to moderate pains.[34] Like all non-opioids, aspirin exhibits a ceiling effect to analgesia.[34] Aspirin shows no evidence of producing tolerance or physical or psychological dependence.[9] Aspirin also has an antipyretic effect.[9]

[9]American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 4th ed. Glenview, IL: American Pain Society; 1999.
[34]Agency for Health Care Policy and Research. *Clinical Practice Guideline No. 9: Management of Cancer Pain.* Rockville, MD: U.S. Department of Health and Human Services; 1994. AHCPR Publication No. 94-0592.

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Agency for Health Care Policy and Research. *Clinical Practice Guideline No. 9: Management of Cancer Pain.* Rockville, MD: U.S. Department of Health and Human Services; 1994. AHCPR Publication No. 94-0592.
American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 4th ed. Glenview, IL: American Pain Society; 1999.

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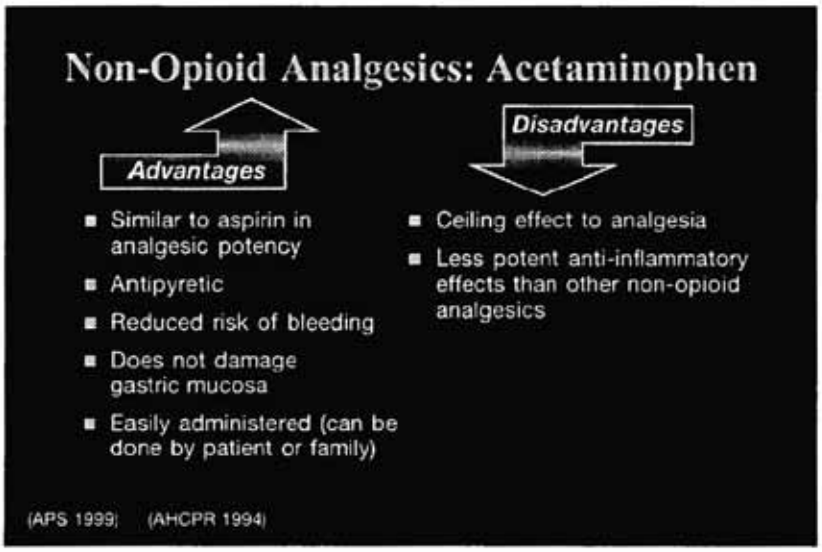

25

Acetaminophen has similar analgesic and antipyretic potency to aspirin.[9] Unlike aspirin, acetaminophen is not associated with bleeding risks or damage to the gastric mucosa.[9] Acetaminophen exhibits fewer anti-inflammatory effects in comparison to other non-opioids.[9,34] Acetaminophen shows no evidence of producing tolerance or physical or psychological dependence.[9]

[9]American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 4th ed. Glenview, IL: American Pain Society; 1999.
[34]Agency for Health Care Policy and Research. *Clinical Practice Guideline No. 9: Management of Cancer Pain.* Rockville, MD: U.S. Department of Health and Human Services; 1994. AHCPR Publication No. 94-0592.

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American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 4th ed. Glenview, IL: American Pain Society; 1999.
Agency for Health Care Policy and Research. *Clinical Practice Guideline No. 9: Management of Cancer Pain.* Rockville, MD: U.S. Department of Health and Human Services; 1994. AHCPR Publication No. 94-0592.

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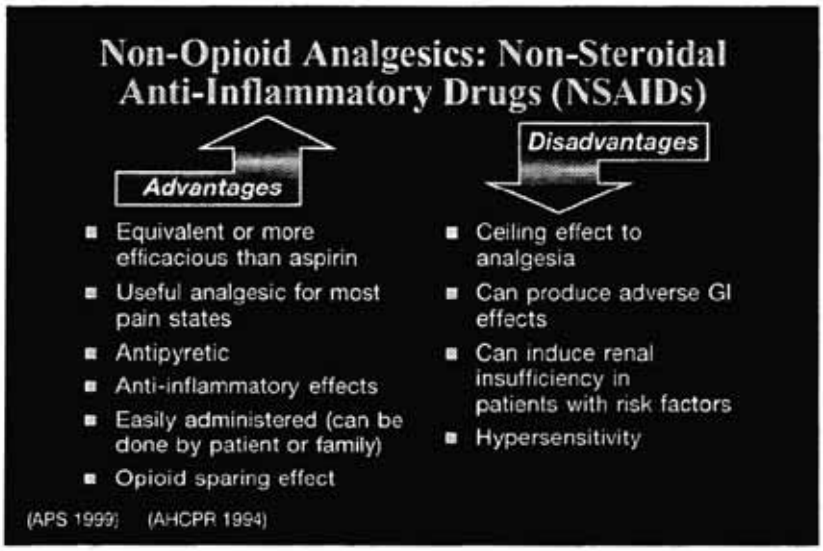

26

NSAIDs are equivalent to or more efficacious than aspirin in analgesic qualities.[9] They are appropriate as initial therapy for mild pain and effective as additive analgesia with opioids and adjuvant analgesics when pain intensity increases.[34] NSAIDs are useful for most pain states, especially those involving inflammation.[9]

Despite their widespread use, NSAIDs may be associated with significant risks. Adverse effects of NSAIDs may include:

- GI toxicities[34]
  - minor: dyspepsia, heartburn, nausea, vomiting, anorexia, diarrhea, constipation, flatulence, bloating, epigastric pain, and abdominal pain
  - major: bleeding, ulceration, and perforation
- Renal insufficiency[9,34]
  - risk factors for NSAID-induced acute renal failure are congestive heart failure, chronic renal insufficiency, cirrhosis with ascites, systemic lupus erythematosus, intravascular volume depletion, diuretics, significant atherosclerotic disease in elderly patients, and multiple myeloma
- Hepatic dysfunction[34]
- Bleeding[34]

[9]American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 4th ed. Glenview, IL: American Pain Society; 1999.
[34]Agency for Health Care Policy and Research. *Clinical Practice Guideline No. 9: Management of Cancer Pain.* Rockville, MD: U.S. Department of Health and Human Services; 1994. AHCPR Publication No. 94-0592.

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American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 4th ed. Glenview, IL: American Pain Society; 1999.
Agency for Health Care Policy and Research. *Clinical Practice Guideline No. 9: Management of Cancer Pain.* Rockville, MD: U.S. Department of Health and Human Services; 1994. AHCPR Publication No. 94-0592.

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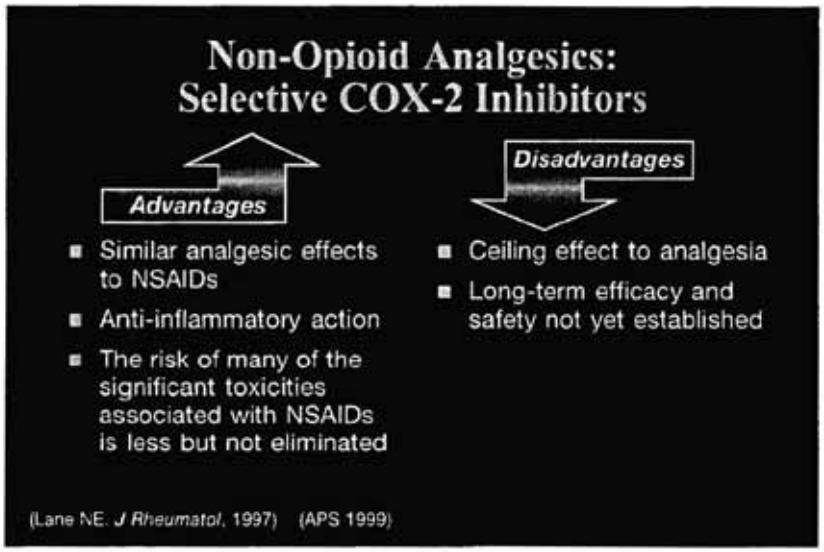

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COX-1 and COX-2 are two isoforms of the enzyme cyclooxygenase.[9] COX-1 is found in blood vessels, the stomach, and kidneys.[9] Inhibition of COX-1 is associated with gastric and renal side effects that can occur with the use of NSAIDs.[9] COX-2 is induced in peripheral tissues by inflammation and leads to further inflammation.[9,35] Inhibition of COX-2 produces therapeutic effects in that it causes a reduction in inflammation.[9,35] The majority of NSAIDs inhibit both COX-1 and COX-2, thereby producing toxic (associated with COX-1 inhibition) and therapeutic (associated with COX-2 inhibition) effects.[9]

Selective COX-2 inhibitors, a group of recently developed compounds, inhibit COX-2 production while causing little inhibition of COX-1.[35] This results in therapeutic efficacy—reduced inflammation—without many of the toxicities associated with NSAID use.[35] Further studies are warranted to demonstrate the long-term efficacy and safety of the COX-2 inhibitors.[9]

[9]American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 4th ed. Glenview, IL: American Pain Society; 1999.
[35]Lane NE. Pain management in osteoarthritis: the role of COX-2 inhibitors. *J Rheumatol* 1997;24(suppl 49):20-24.

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Lane NE. Pain management in osteoarthritis: the role of COX-2 inhibitors. *J Rheumatol* 1997;24(Suppl 49):20-24.
American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 4th ed. Glenview, IL: American Pain Society; 1999.

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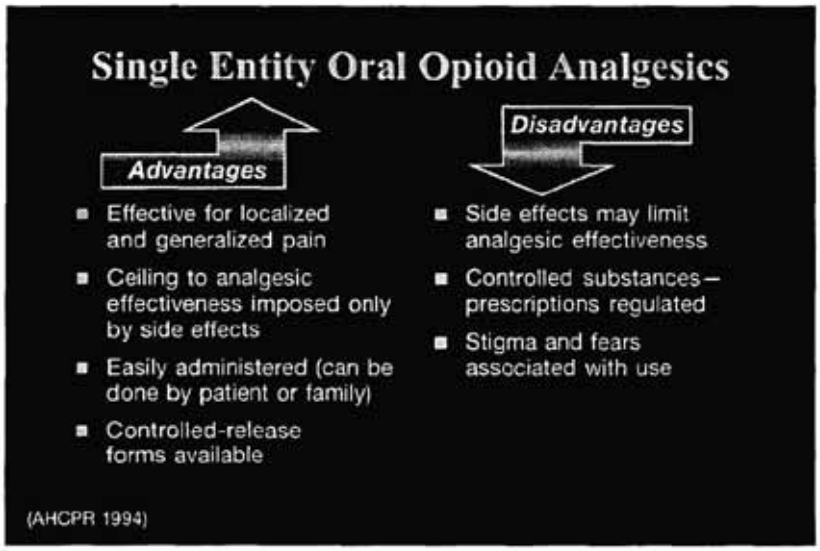

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Opioids are the major class of analgesics used in the management of moderate to severe pain.[34]

- Effectiveness
- Ease of titration
- Favorable risk-to-benefit ratio

Oral opioids have been proven effective for both localized and generalized pain.[34] The analgesic ceiling of these drugs is determined only by the severity of side effects.[34] They are easily administered, and controlled-release forms are available.[34]

One of the disadvantages of opioid use is side effects, which may include sedation, constipation, nausea, vomiting, itching, and respiratory depression.[9,34] Another disadvantage is that opioids are controlled substances which requires that all prescriptions be regulated by law.[34] This often serves as a barrier for healthcare professionals in prescribing opioids because they fear investigation and persecution by medical review boards.[14] A third disadvantage is that opioid use is often associated with exaggerated stigmas and fears.[34]

Oral opioids for severe pain include[9]:

- Morphine
- Hydromorphone (Dilaudid®)
- Oxycodone (OxyContin®)
- Methadone (Dolophine®)
- Levorphanol (Levo-Dromoman®)

[34]Agency for Health Care Policy and Research. *Clinical Practice Guideline No. 9: Management of Cancer Pain.* Rockville, MD: U.S. Department of Health and Human Services; 1994. AHCPR Publication No. 94-0592.
[9]American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain.* 4th ed. Glenview, IL: American Pain Society; 1999.
[14]Holmquist GL. The appropriate use of opioids in the management of chronic pain: a pharmacist's perspective. *Pharmacy Times* 1999;29:3-11.

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Agency for Health Care Policy and Research. *Clinical Practice Guideline No. 9: Management of Cancer Pain.* Rockville, MD: U.S. Department of Health and Human Services; 1994. AHCPR Publication No. 94-0592.

Nonmalignant Pain

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The management of opioid-related side effects is the single most important factor for a successful treatment outcome in pain management.[12] The primary objective in selecting the proper opioid dose for a patient is to achieve a balance between analgesia and side effects.[16]

Common opioid side effects include:

Constipation

- Tolerance does not usually occur[34]
- May be treated prophylactically with the use of stimulant laxatives (bisacodyl, senna) in conjunction with a stool softener (docusate sodium)[12]

Nausea and Vomiting

- Tolerance may develop over two or three weeks[12]
- An antiemetic may be administered to counteract nausea and vomiting[34]

Sedation

- May be counteracted with proper titration or the use of stimulants[12]
- Likely to subside over time[12]

Respiratory Depression

- Patients receiving long-term opioid therapy usually develop tolerance to the respiratory depressent effects of these agents[34]
- Does not occur unless opioids have induced profound sedation[12]
- Careful titration is necessary and short-acting agents should be used for nonambulatory patients with significant pulmonary disease and for patients with documented history of sleep apnea[12]

[12]Pappagallo M, Heinberg LJ. Ethical issues in the management of chronic nonmalignant pain. *Semin Neurol* 1997;17:203-211.
[16]Ellison NM, Lipman AG, Patt RB, Portenoy RK. Opioid analgesia: an essential tool in chronic pain. *Patient Care* 1998:2-11.
[34]Agency for Health Care Policy and Research. *Clinical Practice Guideline No. 9: Management of Cancer Pain.* Rockville, MD: U.S. Department of Health and Human Services; 1994. AHCPR Publication No. 94-0592.

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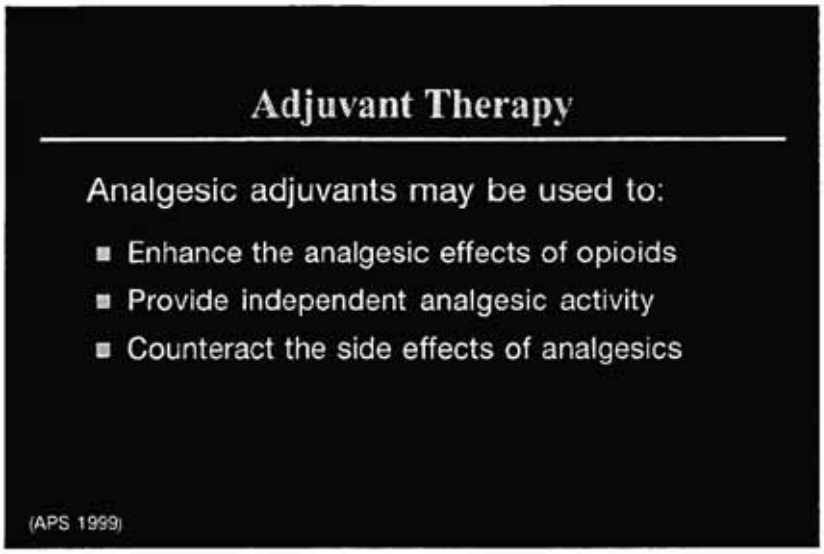

Analgesic adjuvants include[9]:

- Tricyclic antidepressants
- Antihistamines
- Benzodiazepines
- Caffeine
- Dextroamphetamine
- Steroids
- Phenothiazines
- Anticonvulsants
- Clonidine
- Analgesic adjuvants for metastatic bone pain
  - strontium
  - pamidronate

[9]American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain*. 4th ed. Glenview, IL: American Pain Society; 1999.

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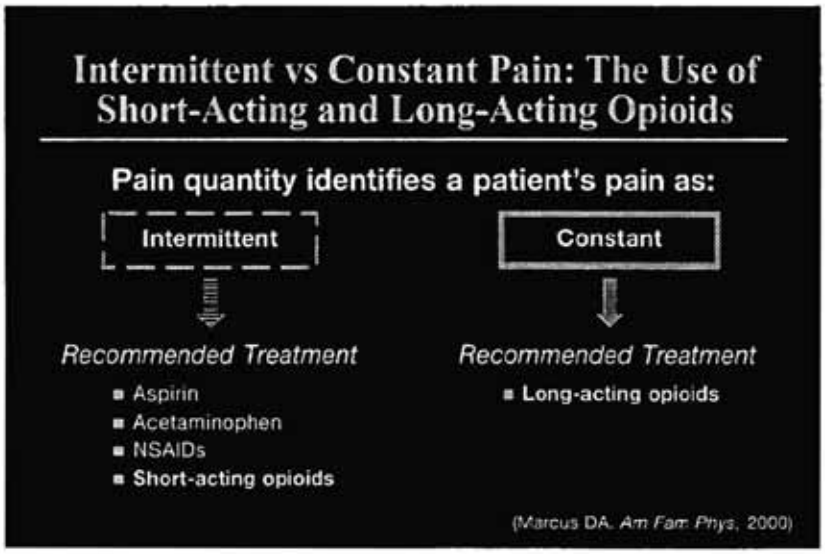

31

Identifying whether a patient's pain is intermittent or constant can assist healthcare professionals in deciding what treatment options should be considered for effective pain management.

Intermittent

Aspirin, acetaminophen, NSAIDs, and short-acting opioids may be used to treat intermittent pain flares.[18]

Constant

Patients with constant pain who may exhibit significant disability or regular analgesic overuse should be considered candidates for treatment with long-acting opioids.[18] Chronic pain sufferers whose treatment regimen includes long-acting opioids generally report "good relief."[18]

[18]Marcus DA. Treatment of nonmalignant chronic pain. *Am Fam Phys* 2000;61:1331-1338, 1345-1346.

Slide Reference

Marcus DA. Treatment of nonmalignant chronic pain. *Am Fam Phys* 2000;61:1331-1338, 1345-1346.

Nonmalignant Pain

Controlled-Release Opioids: Pain Control Around-the-Clock

Controlled-release opioid preparations—among the most important recent innovations in analgesic treatments—help patients to:

- Achieve a steady level of satisfactory analgesia throughout the day
- Sleep through the night
- Enhance compliance

(APS 1999) (Pappagallo M, Heinberg LJ. *Semin Neurol*, 1997)

32

The fundamental concepts of pain management are twofold: 1) provide rapid palliation of current pain and; 2) prevent the occurrence of future pain.[14] The advantages of controlled-release opioids in comparison to short-acting opioids are[14]:

- Extended release of medication over 8 to 12 hours or longer
- Minimal fluctuation in opioid blood levels
- Prevention of many of the peak/trough effects associated with short-acting agents

A clinical study of controlled-release versus immediate-release medications in a long-term care facility found that the use of controlled-release medication may result in[36]:

- Reduced need for medications (patients were kept within their therapeutic range for longer periods of time)
- More nursing time for patients (due to less medication administration time)

A cost-effectiveness analysis of the data revealed that although controlled-release medications are more expensive than immediate-release, the overall cost of therapy with these drugs might be less expensive in the long run. Labor costs associated with more frequent administration of immediate-release medications may exceed the total cost (both labor and drug) of newer controlled-release dosage forms.[36]

[14]Holmquist GL. The appropriate use of opioids in the management of chronic pain: a pharmacist's perspective. *Pharmacy Times* 1999;29:3-11.
[36]Zlotnick S, Prince T, Frenchman IB. Cost analysis of immediate-versus controlled-release medication administration in long-term care. *Consult Pharm* 1997;11:689-692.

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Pappagallo M, Heinberg LJ. Ethical issues in the management of chronic nonmalignant pain. *Semin Neurol* 1997;17:203-211.
American Pain Society. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain*. 4th ed. Glenview, IL: American Pain Society, 1999.

Nonmalignant Pain

OxyContin® C (oxycodone HCl controlled-release) Tablets

Indicated for patients with moderate to severe pain requiring opioid therapy for more than a few days

- **Dosing:** q12h, oral
- **Onset:** Analgesic onset within one hour in most patients
- **Biphasic absorption:** Absorption half-times of 0.6 and 6.9 hours
- **Steady-state levels:** 24 to 36 hours

OXYCONTIN® TABLETS ARE TO BE SWALLOWED WHOLE, AND ARE NOT TO BE BROKEN, CHEWED OR CRUSHED. TAKING BROKEN, CHEWED OR CRUSHED OXYCONTIN® TABLETS COULD LEAD TO THE RAPID RELEASE AND ABSORPTION OF A POTENTIALLY TOXIC DOSE OF OXYCODONE.

Please read the OxyContin® professional prescribing information available with this program

33

OxyContin® (oxycodone HCl controlled-release) Tablets are a controlled-release formulation of oxycodone that are indicated for the treatment of moderate to severe pain requiring opioid therapy for more than a few days.[37] The biphasic absorption profile of OxyContin® allows for the onset of analgesia within one hour for most patients and stable analgesia throughout the 12-hour dosing period.[37]

OxyContin® is a logical choice for the initiation and maintenance of opioid therapy when following a stepwise pain management strategy.[38]

In noncancer patients: A prn opioid or OxyContin® may be appropriate as initial opioid therapy, as judged by the prescriber.

In cancer patients: OxyContin® Tablets may be used as initial opioid therapy for patients no longer responding to or tolerating non-opioids.

When initiating any opioid in opioid-naive patients, significant side effects such as dizziness, nausea, vomiting, and hypotension may be seen in the first days of therapy. Most side effects with OxyContin®, except constipation, diminish over time.

[37]OxyContin® [package insert]. Purdue Pharma L.P.
[38]Data on file, Purdue Pharma L.P., Stamford, CT.

Nonmalignant Pain

Q12h OxyContin® Ⓒ
(oxycodone HCl controlled-release) Tablets

The most serious risk associated with opioids, including OxyContin®, is respiratory depression.

Common opioid side effects are constipation, nausea, sedation, dizziness, vomiting, pruritus, headache, dry mouth, sweating, and weakness.

Please read the OxyContin® professional prescribing information available with this program

34

Nonmalignant Pain

Q12h OxyContin® C (oxycodone HCl controlled-release) Tablets

Contraindications

OxyContin® is contraindicated in patients with known hypersensitivity to oxycodone, or in any situation where opioids are contraindicated. This includes patients with significant respiratory depression (in unmonitored settings or the absence of resuscitative equipment), and patients with acute or severe bronchial asthma or hypercarbia. OxyContin® is contraindicated in any patient who has or is suspected of having paralytic ileus.

Please read the OxyContin® professional prescribing information available with this program

Nonmalignant Pain

Q12h OxyContin® C (oxycodone HCl controlled-release) Tablets

Geriatric Use

- In controlled pharmacokinetic studies in elderly subjects (greater than 65 years) the clearance of oxycodone appeared to be slightly reduced. Compared to young adults, the plasma concentrations of oxycodone were increased approximately 15%.
- In clinical trials with appropriate initiation of therapy and dose titration, no untoward or unexpected side effects were seen based on age, and the usual doses and dosing intervals are appropriate for the geriatric patient. As with all opioids, the starting dose should be reduced to 1/3 to 1/2 of the usual dosage in debilitated, non-tolerant patients.

Please read the OxyContin® professional prescribing information available with this program

Nonmalignant Pain

Q12h OxyContin® Ⓒ (oxycodone HCl controlled-release) Tablets

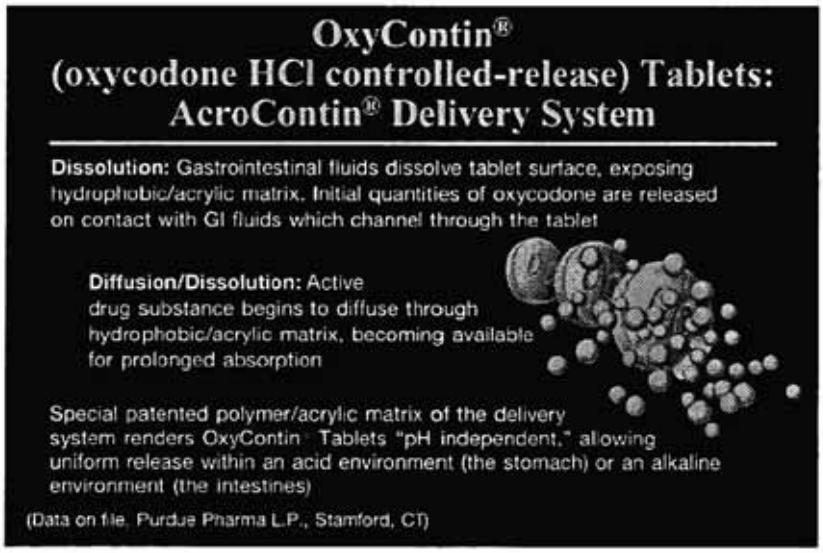
Geriatric Use: Warnings

Respiratory depression occurs most frequently in elderly or debilitated patients, usually following large initial doses in non-tolerant patients, or when opioids are given in conjunction with other agents that depress respiration.

Please see WARNINGS *and* PRECAUTIONS *in OxyContin® professional prescribing information available with this program*

37

Nonmalignant Pain



OxyContin® (oxycodone HCl controlled-release) Tablets employ the patented AcroContin® Delivery System, which includes an innovative dual control matrix formed by two hydrophobic macromolecules and an acrylic polymer that allow for measured release of the active drug.[14] The advantages of the AcroContin® Delivery System of OxyContin® Tablets in comparison to the delivery systems of other controlled-release oral opioids include[14]:

- Bisphasic absorption pattern—provides onset of analgesia within one hour in most patients and effective blood concentrations of oxycodone over a 12-hour dosing interval
- pH independent—allows the uniform release of oxycodone with an acid environment (the stomach) or more alkaline environment (the intestines)

[14]Holmquist GL. The appropriate use of opioids in the management of chronic pain: a pharmacist's perspective. *Pharmacy Times* 1999;29:3-11.

Slide Reference
Data on file. Purdue Pharma L.P., Stamford, CT.

Nonmalignant Pain

OxyContin® (oxycodone HCl controlled-release) Tablets and Nonmalignant Pain Management

- **In noncancer patients:** A prn opioid or OxyContin® may be appropriate as initial opioid therapy, as judged by the prescriber.
- **In cancer patients:** OxyContin® may be used as initial opioid therapy for patients no longer responding to or tolerating non-opioids.
- **When initiating any opioid** in opioid-naive patients, significant side effects such as dizziness, nausea, vomiting, and hypotension may be seen in the first days of therapy. Most side effects with OxyContin®, except constipation, diminish over time.

(Data on file, Purdue Pharma L.P., Stamford, CT)

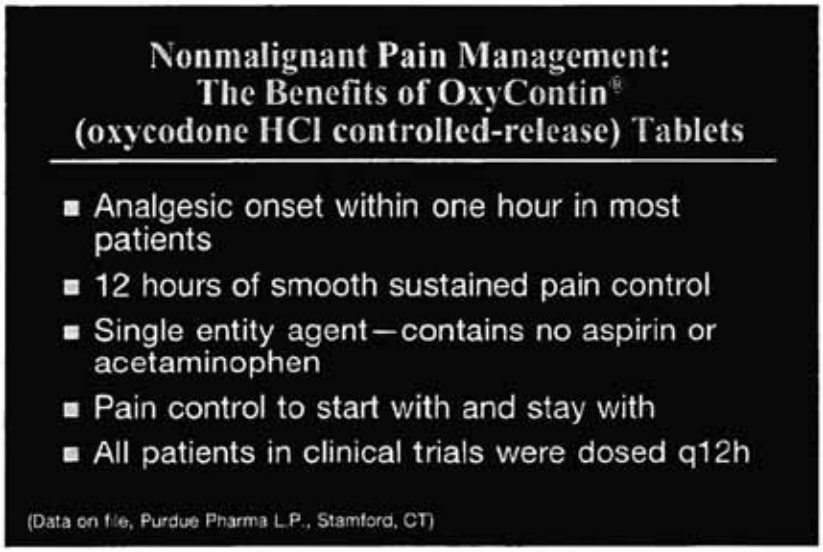
39

A "prn" opioid or OxyContin® (oxycodone HCl controlled-release) Tablets may be appropriate as initial opioid therapy (step 2) in noncancer patients, as warranted by the prescribing healthcare professional.[38] If pain persists, OxyContin® may be continued as long-term maintenance therapy for moderate to severe pain (step 3).[38] The ability to continue the administration of OxyContin® from step 2 throughout step 3 reduces the need for conversion to other opioids.[38]

[38]Data on file, Purdue Pharma L.P., Stamford, CT.

Slide Reference
Data on file, Purdue Pharma L.P., Stamford, CT.

Nonmalignant Pain



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OxyContin® (oxycodone HCl controlled-release) Tablets offer several benefits in the management of nonmalignant pain.

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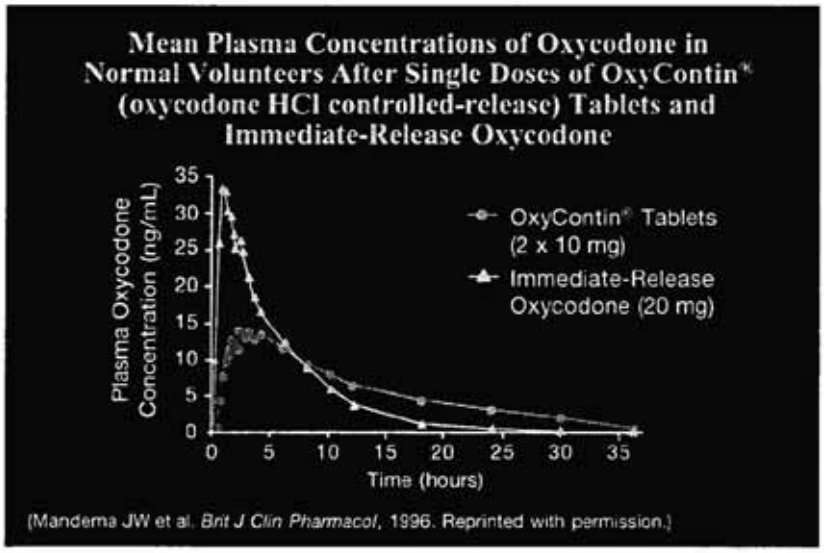
Data on file, Purdue Pharma L.P., Stamford, CT.

Nonmalignant Pain



41

Steady state plasma concentrations of oxycodone are achieved within 24-36 hours of dosing initiation with OxyContin® (oxycodone HCl controlled-release) Tablets.[37]

Controlled-Release Provides Prolonged Relief

The absorption characteristics of OxyContin® allow for effective concentrations to be maintained for a longer period after dosing in comparison to immediate-release oxycodone.[39] OxyContin® provides onset of analgesia within one hour in most patients, followed by a prolonged duration of analgesic activity.[39]

[37]OxyContin® [package insert]. Purdue Pharma L.P.

[39]Mandema JW, Kaiko RF, Oshlack B, Reder RF, Stanski DR. Characterization and validation of a pharmacokinetics model for controlled-release oxycodone. *Brit J Clin Pharmacol* 1996;42:747-756.

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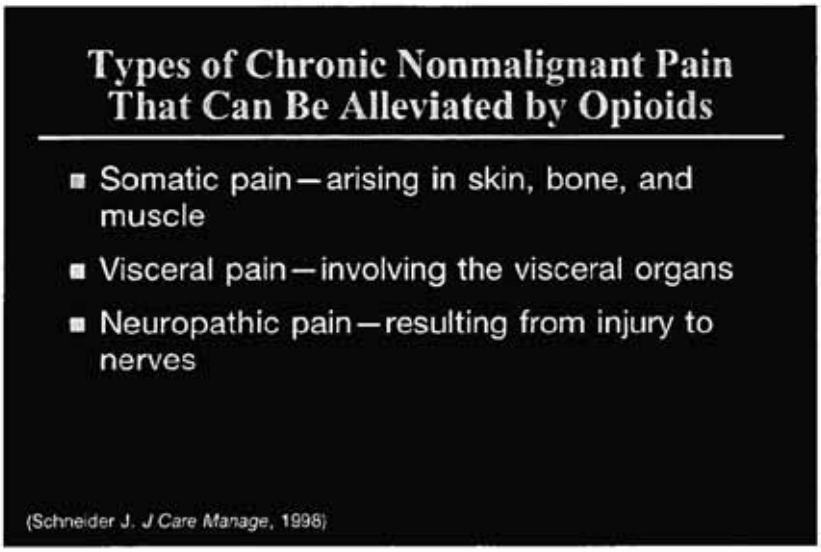
Mandema JW, Kaiko RF, Oshlack B, Reder RF, Stanski DR. Characterization and validation of a pharmacokinetics model for controlled-release oxycodone. *Brit J Clin Pharmacol* 1996;42:747-756.

Nonmalignant Pain



42

Patients with each of the types of pain referenced below have benefited from opioids.[20]

- Somatic pain—arising in skin, bone, and muscle
  - bone and joint pain resulting from injury
  - rheumatoid arthritis
  - osteoarthritis
  - sickle cell anemia
  - chronic osteomyelitis
  - chronic headache
  - chronic back pain related to injury or multiple surgeries
- Visceral pain—involving the visceral organs
  - chronic pelvic pain
  - chronic interstitial cystitis
- Neuropathic pain—resulting from injury to nerves
  - peripheral diabetic neuropathy
  - reflex sympathetic dystrophy
  - post herpetic neuralgia

Pain management strategies for specific nonmalignant conditions will be discussed in the following slides.

[20]Schneider JP. Management of chronic non-cancer pain: a guide to appropriate use of opioids. *J Care Manage* 1998;4:10-22.

Slide Reference

Schneider JP. Management of chronic non-cancer pain: a guide to appropriate use of opioids. *J Care Manage* 1998;4:10-22.

Nonmalignant Pain

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Rheumatoid arthritis (RA) is a form of arthritis that causes inflammation in the lining of the joints and/or other internal organs.[1] Approximately 1% of the U.S. population, or 2.5 million people, have RA.[4] RA[3]:

- Usually begins between ages 25 and 50
- Often develops suddenly, within weeks or months
- Usually affects the same joint on both sides of the body (eg, both knees)
- Causes redness, warmth, and swelling of the joints
- Affects many joints, including elbows and shoulders
- Often causes a general feeling of sickness and fatigue, as well as weight loss and fever

The Arthritis Foundation recommends several medications to control the painful symptoms of rheumatoid arthritis. These include aspirin, NSAIDs, and acetaminophen (by itself or combined with codeine or propoxyphene).[4] Also, joint inflammation can be controlled with corticosteroids combined with aspirin or NSAIDs.[4]

Although opioids are not specifically recommended by the Arthritis Foundation, a study published in *Arthritis & Rheumatism* found that opioids (specifically codeine and oxycodone) significantly reduced pain severity scores in patients with pain related to chronic rheumatic disease.[40] Of the 266 patients in the study on opioid therapy, 64% had a diagnosis of rheumatoid arthritis.[40]

[1]Arthritis Foundation. *Rheumatoid Arthritis* [brochure]. Adanta, GA: Arthritis Foundation; 1998.
[3]Arthritis Foundation. *Osteoarthritis* [brochure]. Atlanta, GA: Arthritis Foundation; 1997.
[40]Ytterberg SR, Mahowald ML, Woods SR. Codeine and oxycodone use in patients with chronic rheumatic disease pain. *Arthritis Rheum* 1998;41:1603-1612.

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Arthritis Foundation. *Rheumatoid Arthritis* [brochure]. Atlanta, GA: Arthritis Foundation; 1998.
Ytterberg SR, Mahowald ML, Woods SR. Codeine and oxycodone use in patients with chronic rheumatic disease pain. *Arthritis Rheum* 1998;41:1603-1612.

Nonmalignant Pain

Pain Management Strategies for Osteoarthritis

- Acetaminophen
- Tramadol
- NSAIDs
- Opioids
- Corticosteroids
- Topical analgesics

❖ *Both controlled-release (CR) oxycodone (q12h) and immediate-release (IR) oxycodone-APAP (qid) were significantly superior to placebo for controlling pain and improving quality of sleep in patients with osteoarthritis*

(Arthritis Foundation 1997) (Caldwell JR et al. *J Rheumatol*, 1999)

Osteoarthritis (OA), sometimes referred to as degenerative joint disease, is the most prevalent muscoskeletal condition that results in joint pain.[35] This condition affects an estimated 16 million Americans.[3] It is more common in men up to age 45; beyond that age it is more common in women.[3] OA[3]:

- Usually begins after age 40
- Usually develops slowly, over many years
- Often affects the joints on only one side of the body at first
- Usually doesn't cause redness, warmth or swelling of the joints
- Affects only certain joints; rarely affects elbows or shoulders
- Doesn't cause a general feeling of sickness

Pain relief is the primary goal of medications used to treat OA.[3] Acetaminophen is often used for pain relief, but it does not reduce swelling or inflammation.[3] Tramadol is being investigated as a pain-relieving agent for older patients who are unresponsive to acetaminophen.[3]

Opioids such as oxycodone, codeine, and propoxyphene are useful for treating acute arthritis pain.[3] NSAIDs help reduce joint pain, stiffness, and swelling.[3] Corticosteroids, injected directly into the joint following aspiration, relieve pain and swelling.[3] The use of corticosteroids should be strictly limited to 3 or 4 injections per year to avoid cartilage damage.[3]

Also helpful in reducing arthritis pain are topical analgesics. These pain-relieving creams may contain salicylates (which decrease the ability of nerve endings to sense pain) or skin irritants (which divert attention away from pain through the stimulation of nerve endings).[3]

Nonmalignant Pain

A double-blind, randomized, multicenter study published in 1999 in the *Journal of Rheumatology* investigated the efficacy and safety of controlled-release oxycodone in the treatment of osteoarthritis pain.[41] OA patients (N = 167) with moderate to severe pain already receiving NSAIDs were randomized to receive controlled-release oxycodone, placebo, or immediate-release oxycodone–acetaminophen for 30 days.[41] Around-the-clock therapy with oxycodone, when added to NSAID therapy, significantly reduced the intensity of moderate to severe OA pain and improved quality of sleep.[41]

[35]Lane NE. Pain management in osteoarthritis: the role of COX-2 inhibitors. *J Rheumatol* 1997;24(suppl 49):20-24.
[3]Arthritis Foundation. *Osteoarthritis* [brochure]. Atlanta, GA: Arthritis Foundation; 1997.
[41]Caldwell JR, Hale ME, Boyd RE, et al. Treatment of osteoarthritis pain with controlled-release oxycodone or fixed combination oxycodone plus acetaminophen added to nonsteroidal anti-inflammatory drugs: a double blind, randomized, multicenter, placebo controlled trial. *J Rheumatol* 1999;26:862-869.

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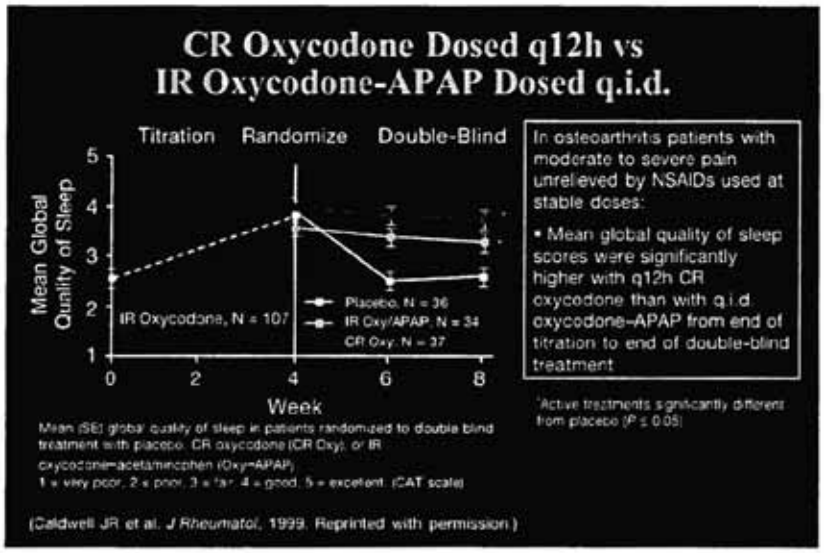
Arthritis Foundation. Osteoarthritis [brochure]. Atlanta, GA: Arthritis Foundation; 1997.
Caldwell JR, Hale ME, Boyd RE, et al. Treatment of osteoarthritis pain with controlled-release oxycodone or fixed combination oxycodone plus acetaminophen added to nonsteroidal anti-inflammatory drugs: a double blind, randomized, multicenter, placebo controlled trial. *J Rheumatol* 1999;26:862-869.

Nonmalignant Pain



45

- Active treatments significantly different from placebo ($P \leq 0.05$).[41]

[41]Caldwell JR, Hale ME, Boyd RE, et al. Treatment of osteoarthritis pain with controlled-release oxycodone or fixed combination oxycodone plus acetaminophen added to nonsteroidal anti-inflammatory drugs: a double blind, randomized, multicenter, placebo controlled trial. *J Rheumatol* 1999;26:862-869.

Slide Reference

Caldwell JR, Hale ME, Boyd RE, et al. Treatment of osteoarthritis pain with controlled-release oxycodone or fixed combination oxycodone plus acetaminophen added to nonsteroidal anti-inflammatory drugs: a double blind, randomized, multicenter, placebo controlled trial. *J Rheumatol* 1999;26:862-829.

Nonmalignant Pain

CR Oxycodone Therapy for Patients With Moderate to Severe Osteoarthritis-Related Pain

- Effective—20 mg q12h CR oxycodone provided a clinically meaningful reduction in pain within 24 hours and was significantly more effective than placebo
- Reduction in the interference of pain relative to placebo with:
  - mood
  - sleep
  - enjoyment of life
- Analgesia maintained during long-term treatment
- Daily dose remained stable after titration
- Typical opioid side effects (eg, nausea, constipation, somnolence)

(Roth SH et al. *Arch Intern Med*, 2000)

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Controlled-release oxycodone therapy provided clinically meaningful, sustained analgesia with a typical opioid side effects profile during short- and long-term treatment of moderate to severe osteoarthritis (OA) pain.[42]

A placebo-controlled fixed-dose trial published in 2000 in *Archives of Internal Medicine* assessed the effectiveness of controlled-release oxycodone for the short- and long-term treatment of moderate to severe pain associated with OA.[42]

- Patients selected for the trial had moderate to severe OA pain and previously had inadequate pain control on prn opioids or NSAIDs
- Patients were randomly assigned to one of three double-blind treatment groups: placebo or 10 mg or 20 mg of controlled-release oxycodone q12h
- 10 mg q12h controlled-release oxycodone was similar to placebo in reducing mean pain intensity
- 20 mg q12h controlled-release oxycodone provided a clinically meaningful reduction in pain within 24 hours and was significantly more effective than placebo

[42]Roth SH, Fleischmann RM, Burch FX, et al. Around-the-clock, controlled-release oxycodone therapy for osteoarthritis-related pain. *Arch Intern Med* 2000;160:853-860.

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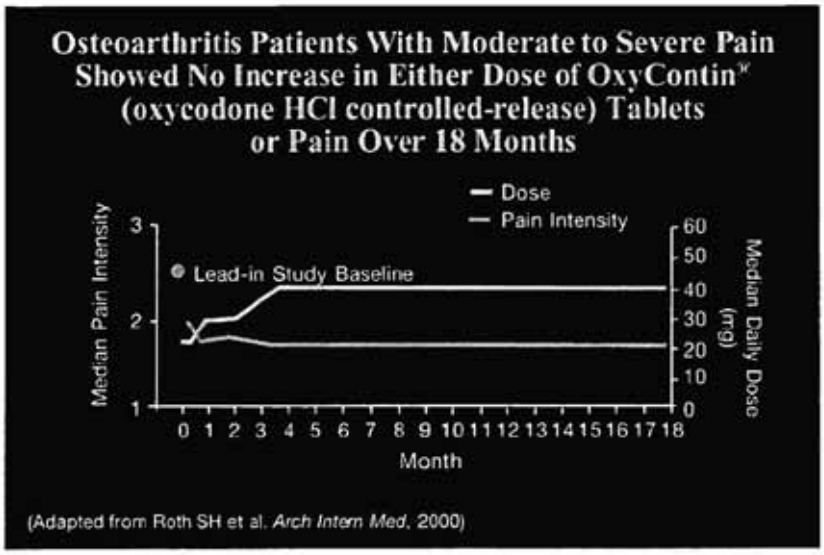
Roth SH, Fleischmann, Burch FX, et al. Around-the-clock, controlled-release oxycodone therapy for osteoarthritis-related pain. *Arch Intern Med* 2000;160:853-860.

Nonmalignant Pain



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Sustained Pain Control, Stable Dosing Over Time

- Analgesia maintained during long-term treatment[42]
- Daily dose remained stable after titration[42]

[42]Roth SH, Fleischmann RM, Burch FX, et al. Around-the-clock, controlled-release oxycodone therapy for osteoarthritis-related pain. *Arch Intern Med* 2000;160:853-860.

Slide Reference

Roth SH, Fleischmann, Burch FX, et al. Around-the-clock, controlled-release oxycodone therapy for osteoarthritis-related pain. *Arch Intern Med* 2000;160:853-860.

Nonmalignant Pain

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Osteoporosis is a disease that causes bones to lose mass and become brittle, leading to painful fractures and possible loss of height and rounded shoulders.[6] Approximately 25 million people in the U.S. are affected by osteoporosis, 80% of which are women.[6]

The Arthritis Foundation and the Osteoporosis Society of Canada both recommend calcitonin for acute, unrelenting, severe pain that results from bone fractures.[6,43] Calcitonin is a naturally occurring hormone approved by the FDA for relieving pain in patients with spine fractures and for controlling bone breakdown.[6]

Bisphosphonates can slow the loss of bone from osteoporosis, restore bone density, and improve bone strength.[6] The first of these drugs to be approved by the FDA for the treatment and prevention of osteoporosis in the U.S. is alendronate.[6] Bisphosphonates are not hormones, and therefore, can be used by women who cannot take estrogen.[6]

Other strategies that may be considered include[6]:

- Increased calcium intake
  - influences bone density
- Regular exercise (that places weight on the bones or increases the force of gravity against them)
  - maintains bone mass
- Estrogen replacement therapy
  - slows the spread of osteoporosis once it has developed
  - reduces fracture risk
  - improves bone mass

[6]Arthritis Foundation. *Osteoporosis* [brochure]. Atlanta, GA: Arthritis Foundation; 1997.
[43]Scientific Advisory Board, Osteoporosis Society of Canada. Clinical practice guidelines for the diagnosis and management of osteoporosis. *Can Med Assoc J* 1996;155(8):1113-29.

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Arthritis Foundation. *Osteoporosis* [brochure]. Atlanta, GA: Arthritis Foundation; 1997.
Scientific Advisory Board, Osteoporosis Society of Canada. Clinical practice guidelines for diagnosis and management of osteoporosis. *Can Med Assoc J* 1996;155:1113-1129.

Nonmalignant Pain

Pain Management Strategies for Sickle Cell Disease

- Moderate to severe sickle cell pain is treated with opioids, with or without NSAIDs, and adjuvant medications
- Sustained-release opioids are recommended for sickle cell patients whose pain requires several days to resolve
  - convenience
  - consistent analgesia
- Other strategies to use in conjunction with analgesic treatment may include:
  - psychological
  - behavioral
  - physical

(APS 1999)

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Sickle cell disease is a group of inherited blood disorders in which hemoglobin S is the dominant hemoglobin and chronic hemolytic anemia and vaso-occlusion are the cardinal pathophysiological features.[44] Pain is the hallmark clinical manifestation of this disease.[44]

Analgesics are the foundation of the management of sickle cell pain and must be tailored according to the duration and severity of the pain experienced by the patient.[44]

Acetaminophen and NSAIDS are recommended for mild-to-moderate pain if there are no contraindications.[44]

- Acetaminophen may be contraindicated in the presence of hepatic failure
- NSAIDS are contraindicated for patients with gastritis, peptic ulcers, coagulopathies, and renal failures

Opioids, with or without NSAIDs, and adjuvant medications are recommended for moderate-to-severe pain.[44]

- Opioids should be administered immediately to emergency room patients with severe pain
- Opioids with a short duration of action are appropriate for patients whose pain lasts for less than 24 hours
- Sustained-release opioids should be administered to patients whose pain persists for several or more days because they provide consistent analgesia and are convenient for patients to use

In conjunction with analgesic medications, the following strategies are recommended for the treatment of sickle-cell pain[44]:

- Psychological: distraction, imagery, education/teaching, hypnotherapy, psychotherapy
- Behavioral: deep breathing, relaxation exercise, self-hypnosis, biofeedback, behavior modification
- Physical: hydration, heat, massage, physical therapy, transcutaneous electrical nerve stimulation (TENS), acupuncture/acupressure

[44]American Pain Society. *Guidelines for the Management of Acute and Chronic Pain in Sickle Cell Disease*. 1999.

Slide Reference

American Pain Society. *Guidelines for the Management of Acute and Chronic Pain in Sickle Cell Disease*. 1999.

Nonmalignant Pain

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The Agency for Health Care Policy and Research issued *Clinical Practice Guidelines Number 14: Acute Low Back Problems in Adults* in December 1994. The AHCPR chose low back pain as a subject for guideline development based on four principal reasons[45]:

- Prevalence—most people report low back problems at some time in their lives
- Cost—low back problems result in substantial economic and psychosocial expenses
- Suboptimal care—evidence shows that many patients with low back problems may be receiving inappropriate care
- Scientific evidence—a growing body of research on low back problems allows for an evaluation of the efficacy and safety of current assessment and treatment methods

A number of medications are effective for controlling back pain. Acetaminophen and NSAIDs are acceptable medication choices for pain relief, although the guidelines express caution in prescribing NSAIDs. Comorbidity, concerns about side effects, and patient and provider preferences should guide the prescribing of these medications.[45] Muscle relaxants are more effective than placebos, but not as effective than NSAIDs.[45] There is no advantage of using muscle relaxants in combination with NSAIDs over using NSAIDs alone.[45]

Opioids are a viable option for acute low back pain over a limited time course.[45] Opioids appear to be as effective as acetaminophen or NSAIDs in relieving back pain when used for a time-limited course of treatment.[45]

Oral steroids, colchicines, and antidepressants are not recommended for the treatment of back pain.[45]

A recent study investigated the use of opioid therapy for chronic back pain. A study published in 1999 in the *Clinical Journal of Pain* compared the efficacy and safety of controlled-release with immediate-release oxycodone in 47 patients with stable, chronic, moderate to severe back pain according to a randomized, double-blind crossover experimental design.[46] Controlled-release oxycodone was just as effective as immediate-release oxycodone in decreasing pain intensity. There were no significant differences in the incidence of side effects between the two study drugs.[46]

Nonmalignant Pain

In addition to pharmacologic management of acute low back pain, other strategies that may be employed include[45]:

Symptom Control: Physical Treatments

- Spinal manipulation—manual therapy in which loads are applied to the spine using short or long lever methods
  Therapeutic objectives: symptomatic relief and functional improvement
- Physical agents and modalities—ice, heat, massage, ultrasound, cutaneous laser treatment, and electrical stimulations (not TENS)
  Therapeutic objectives: symptomatic relief and reduction in inflammation, muscular symptoms, and/or joint stiffness
- Shoe insoles—beneficial for patients with acute low back pain who stand for prolonged periods of time
  Therapeutic objective: reduction of pain
- Lumbar corsets—beneficial for patients with acute low back pain who are required to do frequent lifting at work
  Therapeutic objectives: pain control and/or protection against injury
- Physical treatments **not recommended**: TENS, shoe lifts, spinal traction, biofeedback, and injection therapy (ie, trigger point, ligamentous, facet joint, epidural, acupuncture)

Activity Modification

- Activity recommendations—temporary limitation or avoidance of specific activities known to increase mechanical stress on the spine (eg, heavy lifting, bending, twisting)
  Therapeutic objective: to aid recovery while disrupting daily activities as little as possible
- Bed rest (no more than 4 days)—option for patients with severe initial symptoms of primarily leg pain
  Therapeutic objective: to relieve symptoms by reducing intradiscal pressure and/or pressure on nerve roots
  Prolonged bed rest (more than 2-4 days) appears to be worse for patients than a gradual return to normal levels of activity
- Exercise—back flexion, back extension, generalized strengthening, endurance (aerobic conditioning), and stretching
  Therapeutic objectives: improvements in endurance, muscle strength, and flexibility leading to reduced symptoms, improved level of functioning, and fewer or less severe future back problems

[45]Agency for Health Care Policy and Research. *Clinical Practice Guideline No. 14: Acute Low Back Problems in Adults*. Rockville, MD: U.S. Department of Health and Human Services; 1994. AHCPR Publication No. 95-0642.
[46]Hale ME, Fleishmann R, Saltzman R, et al. Efficacy and safety of controlled-release versus immediate-release oxycodone: randomized, double-blind evaluation in patients with chronic back pain. *Clin J Pain* 1999;15:179-183.

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Agency for Health Care Policy and Research. *Clinical Practice Guideline No. 14: Acute Low Back Problems in Adults*. Rockville, MD: U.S. Department of Health and Human Services; 1994. AHCPR Publication No. 95-0642.
Jamison RN, Raymond SA, Slawsby EA, Nedeljkovic SS, Katz NP. Opioid therapy for chronic noncancer back pain. A randomized prospective study. *Spine* 1998; 23:2591-2600.

Nonmalignant Pain

Pain Management Strategies for Diabetic Neuropathy

- Tricyclic antidepressants (eg, amitriptyline, nortriptyline)
- NSAIDs (eg, ibuprofen, naproxen)
- Anticonvulsants (eg, gabapentin, carbamazepine, valproic acid)
- Benzodiazepines (eg, clonazepam)
- Antiarrhythmics (eg, mexiletine)
- Opioids
- Tramadol HCl
- Dermatological agents (eg, capsaicin)

(Belgrade MJ. *Postgrad Med*. 1999) (Wunderlich RP et al. *South Med J*, 1998)

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Diabetes can affect the peripheral nervous system at all levels and cause neuropathic pain.[47] Symptomatic peripheral neuropathy is the most commonly occurring complication of diabetes.[48] The pain is characterized by lower leg and foot pain that is burning, tingling, lancinating, aching, or tearing.[48,49] This pain can cause disturbances in sleep.[49]

While drug therapy is the standard for diabetic neuropathy, no single agent has been shown to alleviate the painful conditions associated with this disease.[48] Pharmacologic agents that may be used in the treatment of diabetic neuropathy include: tricyclic antidepressants, NSAIDs, anticonvulsants, benzodiazepines, antiarrhythmics, opioids, tramadol HCl, and dermatological agents.[47,48]

Although most opioids are not specifically directed at neuropathic pain, they are potent analgesics that may play a role in controlling intractable neuropathic pain when other measures fail.[47]

[47]Belgrade MJ. Following the clues to neuropathic pain. *Postgrad Med* 1999;106:127-140.
[48]Wunderlich RP, Peters EJG, Bosma J, Armstrong DG. Pathophysiology and treatment of painful diabetic neuropathy of the lower extremity. *South Med J* 1998;91:894-898.
[49]Chan AW. Chronic pain in patients with diabetes mellitus. *Nursing Times* 1991;87:52-53.

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Belgrade MJ. Following the clues to neuropathic pain. *Postgrad Med* 1999;106:127-140.
Wunderlich RP, Peters EJG, Bosma J, Armstrong DG. Pathophysiology and treatment of painful diabetic neuropathy of the lower extremity. *South Med J* 1998;91:894-898.

Nonmalignant Pain

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In addition to drug therapy, healthcare professionals should consider behavioral therapy for patients with painful diabetic neuropathy. This type of therapy includes techniques aimed at promoting relaxation—biofeedback, hypnosis, guided imagery, progressive muscle relaxation, and meditative skills.[47]

[47]Belgrade MJ. Following the clues to neuropathic pain. *Postgrad Med* 1999;106:127-140.

Slide Reference
Belgrade MJ. Following the clues to neuropathic pain. *Postgrad Med* 1999;106:127-140.

Nonmalignant Pain

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Postherpetic neuralgia (PHN) is defined as spontaneous pain provoked by trivial stimuli or altered sensation accompanying herpes zoster and continuing after healing of the characteristic herpes zoster rash.[50] It is a source of great frustration for patients and healthcare professionals.[50] It is characterized by three types of pain: a) steady, often burning pain; b) shock-like lancinating pain; and c) allodynia or pain resulting from normally non-painful stimulation of the skin.[51] Nearly half of PHN patients are totally or partially refractory to the best available therapies.[51] PHN is responsible for 11% to 15% of referrals to pain clinics.[52]

Treatment recommendations for PHN include a topical anesthetic drug (eg, lidocaine) and trials of analgesic and narcotic drugs.[50] Antidepressant or anticonvulsant drugs should be added if the former prove ineffective, inadequate, or poorly tolerated.[50]

Opioids, particularly controlled-release oxycodone, are being increasingly recognized as useful in the management of PHN pain. In a randomized trial investigating the efficacy of controlled-release oxycodone for the management of neuropathic pain published in *Neurology*, 38 patients received either controlled-release oxycodone or placebo every 12 hours over a 4-week study period.[53] Patients receiving controlled-release oxycodone reported significantly greater pain relief, less allodynia, and less paroxysmal spontaneous pain than patients receiving placebo.[53]

In a review of pharmacological treatments for neuropathic pain published in 1999 in the journal *Pain*, the authors found that oxycodone was as effective as tricyclic antidepressants for the treatment of postherpetic neuralgia.[54]

Nonpharmacological methods that may be used to complement pharmacological treatment of PHN include TENS, psychosocial and behavioral approaches.[50]

Nonmalignant Pain

Optional treatment: antiviral drugs

The use of antiviral drugs (eg, acyclovir, famciclovir) in acute zoster is believed to have the potential to prevent chronic PHN pain.[50] The initiation of antiviral therapy is recommended within 72 hours from the onset of zoster rash in order to inhibit viral replication.[51]

[50]Kost RG, Straus SE. Postherpetic neuralgia—pathogenesis, treatment, and prevention. *N Engl J Med* 1996;335:32-42.
[51]Watson CPN. Postherpetic neuralgia: the importance of preventing this intractable end-stage disorder. *J Infect Dis* 1998;178(suppl 1):S91-S94.
[52]Bowsher D. The management of postherpetic neuralgia. *Postgrad Med* 1997;73:623-629.
[53]Watson CP, Babul N. Efficacy of oxycodone in neuropathic pain: a randomized trial in postherpetic neuralgia. *Neurology* 1998;50:1837-1841.
[54]Sindrup SH, Jensen TS. Efficacy of pharmacological treatments of neuropathic pain: an update and effect related to mechanism of drug action. *Pain* 1999; 83:389-400.

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Kost RG, Straus SE. Postherpetic neuralgia—pathogenesis, treatment, and prevention. *N Engl J Med* 1996;335:32-42.
Watson CPN. Postherpetic neuralgia: the importance of preventing this intractable end-stage disorder. *J Infect Dis* 1998;178(suppl 1):S91-S94.
Bowsher D. The management of postherpetic neuralgia. *Postgrad Med* 1997;73:623-629.
Watson CP, Babul N. Efficacy of oxycodone in neuropathic pain: a randomized trial in postherpetic neuralgia. *Neurology* 1998;50:1837-1841.
Sindrup SH, Jensen TS. Efficacy of pharmacological treatments of neuropathic pain: an update and effect related to mechanism of drug action. *Pain* 1999; 83:389-400.

Nonmalignant Pain

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Although the role of opioids in chronic nonmalignant pain is rapidly evolving, further research is warranted to establish guidelines on[33]:

- How to select patients
- How to select the right drug
- How to titrate the drug
- How to manage side effects
- How to appropriately monitor the outcomes in chronic nonmalignant pain, including outcomes related to chemical dependency
- How to add drugs to the opioids to maximize benefit and minimize risk by improving the balance between analgesia and adverse effects

[33]Portenoy RK. Current pharmacotherapy of chronic pain. *J Pain Symptom Manage* 2000;19:S16-S20.

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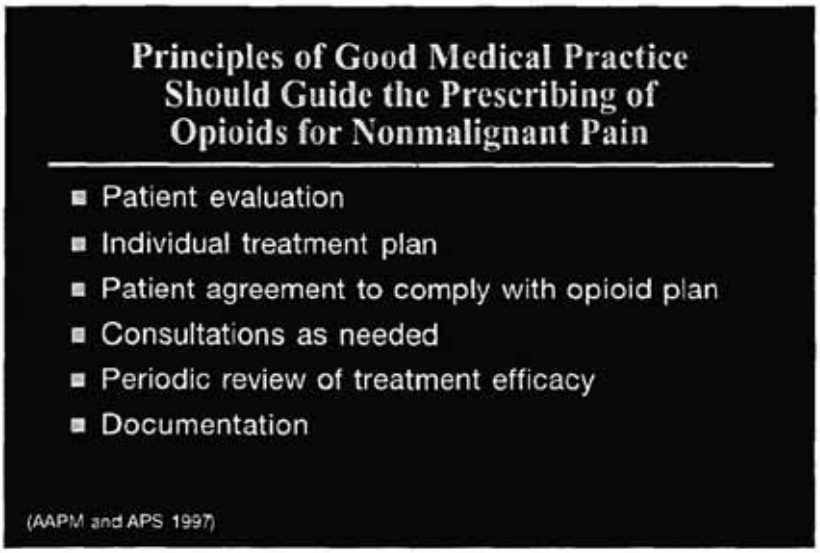
Schneider JP. Management of chronic non-cancer pain: a guide to appropriate use of opioids. *J Care Manage* 1998;4:10-22.

Nonmalignant Pain



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The AAPM and APS consensus statement on the use of opioids for the treatment of chronic pain recommends that principles of good medical practice should guide the prescribing of opioids. These principles include[28]:

- Patient evaluation—including a pain history, an assessment of pain's impact on the patient, a directed physical examination, review of previous diagnostic studies, drug history, and an assessment of comorbidities.
- Treatment plan tailored to the individual and the presenting problem. An opioid trial should not be done in the absence of a complete assessment of the pain complaint. The patient or patient's guardian should be fully informed of the risks, goals, and benefits of opioid therapy. A written agreement is often helpful.
- Consultation with specialists in pain medicine or psychologists as needed.
- Periodic review of treatment efficacy, including functional status of the patient, analgesia, side effects, quality of life, and indications of medicine misuse.
- Documentation—written documentation is essential to support the evaluation, clinical indication for opioid use, pain management treatment plan, consultations, and periodic reviews of the patient's status.

[28]American Academy of Pain Medicine and American Pain Society. The use of opioids for the treatment of chronic pain [consensus statement]. Glenview, IL: American Academy of Pain Medicine and American Pain Society; 1997.

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American Academy of Pain Medicine and American Pain Society. The use of opioids for the treatment of chronic pain [consensus statement]. Glenview, IL: American Academy of Pain Medicine and American Pain Society; 1997

Nonmalignant Pain

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In a perfect world, healthcare professionals rely on science to support their approach to clinical practice and in establishing professional standards of care.[11] Until there is further clinical research aimed at defining the appropriate long-term use of opioids for chronic nonmalignant pain, healthcare professionals will continue to rely on a combination of scientific, social, political, religious, and legal concerns to guide their prescribing practices.[11]

Until more research is available, healthcare professionals should:

- Recognize the importance of overcoming "opiophobia"
- Define a comfort level with opioids
- Develop a set of standards to guide opioid use and follow them on a regular basis

[11]Turk DC, Brody MC, Okifuji EA. Physicians' attitudes and practices regarding the long-term prescribing of opioids for non-cancer pain. *Pain* 1994;59:201-208.

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Pappagallo M, Heinberg LJ. Ethical issues in the management of chronic nonmalignant pain. *Semin Neurol* 1997;17:203-211.
American Academy of Pain Medicine and American Pain Society. The use of opioids for the treatment of chronic pain [consensus statement]. Glenview, IL: American Academy of Pain Medicine and American Pain Society; 1997

Nonmalignant Pain

(cont'd)

Nonmalignant Pain Management With Opioids: A Review of the Critical Issues

Witness the Results

- The use of opioids for the treatment of nonmalignant pain is a legitimate treatment in the step progression of pain management
  - long-acting opioids administered around-the-clock should be considered in patients who have a clear pain diagnosis, constant pain, pain with significant disability, or regular analgesic overuse
- The role of opioids in chronic nonmalignant pain is rapidly evolving

(Schneider J. *J Care Manage*, 1998) (Marcus DA. *Am Fam Phys*, 2000) (Portenoy R. *J Pain Symptom Manage*, 2000)

The role of opioids in the management of chronic nonmalignant pain is rapidly evolving.[33] Recent studies have shown that opioids can be taken by patients with chronic pain on a relatively long-term basis with satisfactory results.[55]

A 1998 study examining 19 patients receiving long-acting opioid medications for the treatment of chronic pain not related to cancer found the following[56]:

- Significant decrease in pain intensity
- Decrease in ratings of impairment due to pain
- Reduction in anxiety and hostility
- Differential improvement in sleep
- No decline in cognitive function
- Improved measure of sustained attention and psychomotor speed

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